ABSTRACTS OF WORLD MEDICINE

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Hygiene and Public Health

1335. **Studies on Mass Control of Dental Caries through Fluoridation of the Public Water Supply**
H. T. DEAN, F. A. ARNOLD, P. JAY, and J. W. KNUTSON. *Public Health Reports* [*Publ. Hlth Rep., Wash.*] **65**, 1403–1408, Oct. 27, 1950. 1 fig., 3 refs.

Fluoridation of the Grand Rapids public water supply began in January, 1945. Analysis of the 1949 dental examinations at Grand Rapids shows a reduced amount of dental caries experience when compared with the pre-fluoridation rates of 1944–5. The findings indicate that the reduction is most pronounced in the younger age groups whose dentition was largely calcified following the addition of one part per million of fluoride to the previously fluoride-free public water supply. Sufficient time has not elapsed to evaluate water fluoridation in the older age groups.—[Authors' summary.]

1336. **The Significance of Mental Hygiene in a School Medical Service.** (Die Bedeutung der psychischen Hygiene im Schulgesundheitsdienst)
G. F. ANDREWS and F. A. HEIMANN. *Gesundheit und Wohlfahrt* [*Gesundh. u. Wohlf.*] **30**, 423–431, Sept., 1950. 3 refs.

The authors emphasize the importance of mental hygiene in a school medical service; only by the constant co-operation of teacher, school medical officer, and psychiatrist can an effective medical service be secured in schools. Although in routine group examinations the school medical officer cannot easily diagnose mental disturbances without somatic symptoms, he has opportunities for repeated examination and observation of progress in individual cases. With the help of a psychiatric specialist it is possible to discover underlying emotional disturbances giving rise to symptoms such as backwardness, incipient delinquency, stammering, and enuresis. The authors describe the cases of 5 children who were referred to the Psychiatric Polyclinic, Royal Victoria Hospital, Bournemouth, as being backward in school. Their I.Q. was, however, relatively high and subsequent investigation disclosed hidden neuroses, sometimes even engendering somatic symptoms. As a result of psychotherapy their progress and adjustability improved.

School medicine should in any case be of a psychosomatic character, taking into account not only somatic symptoms, but also such factors as physical and psychic constitution, heredity, past history, home environment, and school influences. All suspect children should be examined separately for exogenous and endogenous factors; only this can show whether their trouble is due to some organic disease or is due to some emotional disturbance. The present artificial distinction made under the British school medical service, by which retarded children fall under the care of the school medical officer while those with definite psychosomatic disorders are sent to a psychiatric clinic, is harmful to the latter. Constant co-operation is strongly advised between school medical officer and psychiatric specialist, who should enlist the help of the teacher and of the parents in their investigations. *Catherine Schöpflin*

1337. **Social and Psychological Factors Affecting Fertility. X. Fertility Planning and Fertility Rates by Religious Interest and Denomination**
K. FREEDMAN and P. K. WHELPTON. *Milbank Memorial Fund Quarterly* (*Milbank mem. Fd Quart.*) **28**, 294–343, July, 1950. 11 refs.

This paper records the result of an investigation that was designed to examine the hypothesis that " the greater the interest in religion, the lower the proportion of couples practising contraception effectively and the larger the planned families ". Reference is made to previous American and British studies, certain of which have shown that marked differences exist between the fertility rates of Catholics, Protestants, and Jews living within one and the same national group, while others have shown the family size to be related to some extent to the religious training and observance of the parents, irrespective of religious denomination. The authors also call attention to the common assumption that there must necessarily be a definite connexion between the place of religion in individual and community life and the high fertility rates that obtain amongst the peoples of the Far East and of similar pre-industrial areas.

In the present study, based on information obtained by interview from 860 " relatively fecund " white Protestant couples living in Indianapolis, it was found that although there was a direct relationship between religious interest and fertility, this became manifest only when the extreme degrees of religious interest were compared and no regular gradation of fertility was evident in the intermediate categories. Fertility varied with religious denomination, and those denominational groups with the highest fertility contained the lowest proportion of couples whose families were planned as to spacing, or numbers, or both, a notable exception being the Christian Science group, which had the lowest fertility rate but occupied an intermediate position in respect of family planning.

On the whole the findings do not indicate that religious interest is of great importance in explaining variations in

reproductive behaviour. It is emphasized, however, that these conclusions apply only to a limited sample of the American population, a group of urban, native-white Protestants with at least a complete grammar-school education. *F. A. E. Crew*

1338. **Poliomyelitis and River Bathing.** (Poliomyélite et bains de rivière)
J. Boyer and M. Tissier. *Presse Médicale* [*Pr. Méd.*] **58**, 1183–1186, Oct. 25, 1950. 3 figs., 6 refs.

A serious outbreak of poliomyelitis which occurred in France during the summer of 1949 brought forward the question of river bathing as a possible source of infection. In certain prefectures it was decided to impose a total ban on river bathing, a decision vigorously disputed by various sports organizations. The authors have undertaken a statistical investigation in order to determine to what extent river pollution can be incriminated as a serious source of danger when poliomyelitis is prevalent. Their general conclusion is that river bathing plays only a very minor role in the dissemination of infection. In a series of 767 cases notified during the period 1943–9 they found that the proportion of cases occurring in those age groups in which river bathing is most commonly practised showed no increase during the summer months when such activities are most in vogue; during spring, autumn, and winter the distribution of 352 cases was as follows: (1) Children of pre-school age (0 to 6 years), 38%. (2) Children of school age (7 to 14), 22%. (3) Adolescents (15 to 21), 17%. (4) Young adults (22 to 40), 19%. (5) Over 40 years, 4%. The corresponding summer figures (415 cases) were as follows: (1) 34%, (2) 19%. (3) 21%. (4) 22%. (5) 4%.

The authors suggest that certain cases of acute poliomyelitis which have been reported within a day or two of bathing in a river may be due to activation of a pre-existing latent infection owing to immersion in cold water and the exercise of swimming. Nevertheless they point out that many rivers in France are heavily contaminated with faecal matter and suggest that in epidemics bathing in chlorinated pools is certainly much safer. They do not advise any general ban on river bathing, but agree that it is undesirable in those localities where the disease is prevalent. Measures are in hand in France to reduce river pollution, but even as things are at present they regard this factor as of quite minor importance in the spread of poliomyelitis. *Joseph Ellison*

1339. **Control of Norway Rats with Residual Rodenticide Warfarin**
W. J. Hayes and T. B. Gaines. *Public Health Reports* [*Publ. Hlth Rep., Wash.*] **65**, 1537–1555, Nov. 24, 1950. 2 figs., 10 refs.

Poisons hitherto used as rodenticides have generally been substances which are lethal in single doses of appropriate strength, but which all give rise, to a greater or less extent, to bait shyness in the animals to be killed. In this report an account is given of the use of a new chemical rodenticide, " warfarin " (3-(α-acetonylbenzyl)-4-hydroxycoumarin), which kills effectively only when consumed repeatedly and produces no acquired bait refusal. Laboratory tests were first carried out on healthy caged rats which were given the poison by stomach tube daily or on alternate days, and showed that warfarin could kill 90% or more of the rats in 2 to 12 days when given in a total dosage of 5 mg. per kg. body weight. In simulated field experiments with wild Norway rats there was no indication of bait shyness, the consumption of poisoned bait being no less rapid than that of poison-free food. Very low concentrations of poison in the bait were effective, there apparently being no advantage in using more than 0·05 mg. per g. of food. When the poison was used in the field, rat infestations of various types of food-store were controlled within 2 or 3 weeks, some of the establishments remaining rat-free for a month or longer after withdrawal of the warfarin; reappearance of rats was the result of reinfestation. Warfarin was used successfully in places in which treatment with " 1080 " or " ANTU " had not proved satisfactory.

The requirements of an ideal rat poison, as stated by O'Connor (*Research*, 1948, **1**, 334) and modified by the present authors, are as follows: " (1) The poison must be surely effective when incorporated into baits in such small quantity that its presence is not detected to an interfering degree. (2) Finished baits containing the poison must not excite bait shyness in any way and the necessity of prebaiting must, thereby, be avoided. (3) The manner of death must be such that surviving individuals will not become suspicious of its cause, but will remain on the premises and eat freely of the bait until they themselves die. (4) The poison, in the concentration used for control, must be specific for the species to be destroyed unless its use can be made safe for man and domestic animals by some other means ". The first three of these requirements are fully met by warfarin, and the fourth more nearly than by any effective single-dose rat poison at present available. Although some of the rats died in places where they could not be reached, any odours noticed were not more frequent or stronger than those expected when other poisons are used. No difficulty was experienced in getting the rats to enter the bait stations. The costs of operation, including the construction of bait stations and removal of dead rats, were not high. *Caryl Thomas*

VITAL STATISTICS

1340. **Contemporary Tendencies in Spanish Infant Mortality.** (Tendencia contemporanea de la mortalidad infantil española)
J. Villar Salinas. *Revista de Sanidad e Higiene Pública* [*Rev. Sanid. Hig. públ., Madr.*] **24**, 605–650, Sept., 1950. 30 figs., 26 refs.

At the beginning of this century the infant mortality in Spain amounted to 175 per 1,000 live births; this figure showed a considerable decrease to 64 per 1,000 by 1948. After the civil war the rate went up to 135 in 1939; in 1941, due to economic difficulties and to deterioration of nutritional standards, the figure became 143 per 1,000 live births. In 1949 there was again a slight rise in

infant mortality, which reached 68 per 1,000. By comparing the monthly rates for the years 1942 to 1949, the author found that most babies died in the summer months (June to August), with a maximum death rate in July, mainly as a result of gastro-intestinal disturbances. In recent years the figure has decreased on account of improvement in sanitary conditions. The death rate from immaturity and congenital malformations has remained stationary during the last 50 years. [Those particularly interested in Spanish vital statistics and comparison with those of other countries should read the entire paper; the figures and calculations do not lend themselves to abstracting.] *Franz Heimann*

1341. **Mortality from Diphtheria: the Recent Trend Compared with Scarlet Fever, Whooping Cough and Measles**

W. P. D. LOGAN. *Medical Officer* [*Med. Offr*] **84**, 217–219, Nov. 18, 1950. 4 figs.

The mortality from diphtheria, in common with that of other infectious diseases of childhood, has been declining since the beginning of the century. Although it is generally accepted that the very large fall in mortality from diphtheria during the past decade has been due to the immunization campaign, there are some who maintain that the total decline in mortality from diphtheria over the past 50 years is not very different from that in respect of the common infectious diseases of childhood against which there has been no large-scale immunization The author has therefore compared the trends of mortality from diphtheria, scarlet fever, whooping-cough, and measles in England and Wales during the last 85 years. The comparison was made by constructing for each disease a second-order logarithmic curve from the quinquennial death rates at ages under 15 years from 1866–70 to 1936–40, and extrapolating to 1949 to show the mortality which would have been expected had the trend from 1866 to 1940 been maintained, the observed mortality in each year being plotted side by side with the expected mortality.

The curve of observed mortality from whooping-cough during 1941–9 was in very close agreement with the extrapolated curve, showing that the rate of decline has not been disturbed by the introduction of any new factor since 1940. The observed rates for measles after 1940 were, however, somewhat less than the calculated rates, and during 1948 and 1949 were only about half the expected values, being 23 and 30 per million respectively. The mortality trends of both scarlet fever and diphtheria showed considerable departure from the expected trend during 1941–9, and for botn diseases the observed death rates have declined farther and farther below the calculated values. In 1949 the actual mortality from scarlet fever (1·4 per million) was only one-tenth, and that from diphtheria (7·1 per million) only $\frac{1}{22}$, of the value calculated from earlier mortality trends. The similarity of the recent trends of scarlet fever and diphtheria mortality was not due to the operation of similar factors. Notifications of cases of scarlet fever fell by 11% between 1938–40 and 1949, while the notifications of diphtheria fell by 91% during the same period. Thus the fall in the death rate from scarlet fever has been due to a decreased fatality rather than to decreased incidence, whereas with diphtheria the fall in the death rate has been due largely to the fall in the case incidence, accompanied by a reduction in fatality comparable to that in scarlet fever.

It is thus clearly demonstrated that since the introduction of widespread immunization against diphtheria late in 1940 the mortality from diphtheria has been reduced to a far greater extent than that from whooping-cough and measles, and in a manner quite different from that in which mortality from scarlet fever has been reduced.

W. J. Martin

1342. **Incidence of Cancer in American Males. 15,000,000 Man-years of Aggregate Experience, United States Army, 1944–1945**

D. LINDSEY and E. M. COHART. *Cancer* [*Cancer*] **3**, 945–959, Nov., 1950. 2 figs., 3 refs.

The authors have made use of the United States Army medical records of casualties resulting from illness or injury during the two years 1944 and 1945 to estimate the incidence of cancer in a population which, in respect of males between 20 and 40 years of age, is probably the largest ever studied. Estimation of the incidence of cancer among the general population is difficult, and the figures available have been mainly derived from the analysis of mortality statistics. Moreover, there are problems of determining the size and age distribution of the population from which the cancer cases are drawn and the degree of accuracy with which such cases are reported which do not arise in connexion with military statistics. For this reason it is probable that the results obtained by the authors represent the closest approximation to the true incidence that has yet been made.

Estimations were first made on the basis of a 20% sample of all cases of malignant disease diagnosed in each year among white males, and a further estimation made on the basis of the total number of such cases for 1944 only. The incidence of cancer (including lymphoma and leukaemia) per 100,000 white males per annum according to this last estimation was as follows: less than 20 years of age, 12·67; 20 to 24, 16·47; 25 to 29, 26·51; 30 to 34, 43·57; 35 to 39, 67·75; 40 to 44, 144·31; and 45 or more years of age, 289·83. The incidence, in each age group, of cancer in 25 anatomical sites and of 11 histological types was also calculated. The over-all figures were compared with those obtained in two surveys of large civilian populations, which were found in general to be higher.

[For details of the anatomical and histological analysis and of the methods used the original paper should be consulted.] *W. J. Martin*

1343. **Cancer Mortality in Australia**

H. O. LANCASTER. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 501–506, Sept. 30, 1950. 2 figs., 4 refs.

The deaths from all forms of cancer recorded in Australia between 1908 and 1945 are analysed and subdivided by sex and age. In the last quinquennium, 1941–5, the proportions of all deaths which were considered due to cancer were as follows: up to 14 years,

about 0·6% in each sex; ages 15 to 44, 6% male, 11% female; ages 45 to 74, 14% male, 20% female; ages over 75, 10% male, 9% female. Analysis of the 1908–45 death rates at various ages reveals no appreciable change in rates in childhood and early adult life (ages under 35), a decline in mortality in both sexes at the important ages of 35 to 44, 45 to 54, and 55 to 64, and a rise only in the age groups 65 to 74 and 75+. At these ages increased precision in diagnosis may well be a factor in the rise. In total, there has been no certain increase in cancer mortality in Australia over the period studied, though the ageing of the population has inevitably brought about an increase in the crude death rate, and this increase will continue in the future. The age-specific death rates per million in 1911–20 and 1941–5 were as follows:

Age	Males		Females	
	1911–20	1941–45	1911–20	1941–45
0—	25	28	19	26
15—	33	35	31	39
25—	98	92	148	139
35—	351	278	648	574
45—	1,396	1,049	1,805	1,549
55—	3,762	3,160	3,447	3,170
65—	7,006	7,995	5,757	6,315
75+	9,990	14,678	8,713	10,813
Crude rate	808	1,180	771	1,215

A. Bradford Hill

EPIDEMIOLOGY

1344. **Q Fever in Great Britain. Epidemiology of an Outbreak**
B. P. MARMION and M. G. P. STOKER. *Lancet* [*Lancet*] **2**, 611–616, Nov. 25, 1950. 2 figs., 13 refs.

Epidemiological investigation of an outbreak of Q fever at the Royal Cancer Hospital, London, showed the source of infection of cases occurring among the staff to be a patient who was admitted during the incubation period of the disease and who subsequently died of it. Examination of this patient's home environment in north-east Kent revealed that his household was supplied with raw milk, from which *Rickettsia burnetii* was isolated. Blood samples from a proportion of the cattle and farm workers on 3 of the 7 farms supplying the milk, and of the workers in 3 retail dairies concerned in its distribution, gave positive results in agglutination tests against *R. burnetii*. A second outbreak of Q fever occurred at the hospital shortly after the first, but the 2 patients (an employee of the hospital and his wife) were considered most probably to have been infected while staying at a farm in Devon, since cattle there were later shown to give positive serological reactions, while another visitor to the farm had subsequently developed serologically proven Q fever.

[The original paper should be read for its critical and detailed account of the steps leading to the recognition of another endemic milk-borne disease in this country. (See also MacCallum *et al.*, *Lancet*, 1949, **2**, 1026 and Harman, *Lancet*, 1949, **2**, 1028).]

J. E. M. Whitehead

1345. **Poliomyelitis. Epidemiological Study, Prophylaxis, and Treatment.** (Poliomielitis. Estudio epidemiologico, profilaxis y tratamiento)
J. L. MORALES. *Acta Pediátrica Española* [*Acta pediátr. esp.*] **8**, 1141–1159, Oct., 1950. 6 figs.

The majority of poliomyelitis cases in the Seville area during the last outbreak were observed in the winter months, the epidemic reaching its peak in May, 1950, whereas a previous epidemic (1939) began in July and August. The incidence of cases was higher in towns than in villages. Although the author cannot yet give more details, he is of the opinion that the infection may be connected with the intake of infected milk, water, or raw fruit and vegetables. He advocates an energetic campaign against flies, improvement of hygiene in stables, provision of cleaner water and food, and disinfection of faeces with calcium hypochlorite. During an epidemic schools should be closed and tonsillectomy, extraction of teeth, and vaccination should not be performed. As preventive measures he recommends the boiling of milk and water and the cooking of vegetables before consumption. Children should avoid excessive exposure to the sun or to drenching rain, and abstain from long walks and over-exertion.

Franz Heimann

1346. **A Contribution to the Study of Leptospirosis Grippo-typhosa. A Summer Epidemic Affecting 77 Members of a Military Community.** (Contribution à l'étude de la leptospirose à *Leptospira grippo-typhosa*, fièvre des marais, fièvre de la vase. Une épidémie estivale de 77 cas en milieu militaire)
R. A. LEFEBVRE DES NOETTES, C. SEIGNEURIC, and B. KOLOCHINE-ERBER. *Presse Médicale* [*Pr. méd.*] **58**, 1189–1192, Oct. 25, 1950. 3 figs., 11 refs.

The authors describe an epidemic of leptospirosis grippo-typhosa which affected 77 young soldiers in the summer of 1949. The infection was incurred through bathing in a stagnant pool containing a thick layer of mud which was disturbed by diving exercises. The *p*H of the water (7·5) and the unusually high temperature obtaining at the time were regarded as predisposing factors in this epidemic. Leptospira of a type non-pathogenic for the guinea-pig were isolated in culture from the water. The clinical manifestations in this outbreak were uniformly benign, though initial meningeal symptoms were sometimes severe, and general weakness and a feeling of exhaustion remained for some months after cure had been effected. Diagnosis was reached in all cases by means of serum agglutination, which became positive on about the 12th day and remained so for some months. Leptospira (unclassified) were recovered from the blood in a few cases after 10 days' incubation, by which time all symptoms had disappeared. As this particular form of leptospirosis is benign and rapidly self-terminating no special therapeutic measures were called for, but the authors consider that intravenous

hypertonic saline was useful in 3 cases with severe cerebral symptoms. Lumbar puncture was not performed. They point out the considerable difficulties which may arise in the diagnosis of isolated cases of leptospirosis. [In Great Britain such cases would be confidently diagnosed as abortive poliomyelitis.] The authors consider that leptospirosis (Dimitrov) is probably a more common disease in France than is realized, and suggest that bathing in stagnant pools be forbidden. *Joseph Ellison*

1347. **An Epidemic of Leptospirosis in Pea-pickers.** (Eine Feldfieberepidemie bei Erbsenpflückern)
L. POPP. *Zeitschrift für Hygiene und Infektionskrankheiten* [*Z. Hyg. InfektKr.*] **131**, 575–601, 1950. 7 figs., 15 refs.

An epidemic of leptospirosis occurred in pea-pickers between July 20 and August 10, 1949, in a south-east Brunswick rural district. The infection was shown to be due to *Leptospira grippotyphosa*, which had caused an epizootic in field-mice in the same region at the same time. The epidemic and the epizootic ran parallel. Climatic conditions exerted an influence: June had been a very wet month; the period under investigation was unusually dry. It is suggested that the epizootic, favoured by the wetness in June, had preceded the epidemic. The leptospira index of field-mice was as high as 80% in one field. Hamsters also appeared to be affected. The morbidity in pea-pickers averaged 3%, though in the field where the highest index for mice was recorded it reached 25%. Of the clinical symptoms, enlargement of the spleen, headache, meningeal symptoms, and conjunctival irritation were universally present; measles-like eruptions were reported, and albumin, casts, and erythrocytes never failed to appear in the urine after the 4th day of illness. The pathological characteristics in mice were acute or subacute glomerulonephritis, cell infiltrates in the liver, and periarterial cell infiltrates in the lung. Fusiform bacilli were often found in the kidneys. In experienced hands the diagnosis of leptospirosis in mice could be made macroscopically. The golden hamster appeared to be a suitable experimental animal for study of leptospirosis grippotyphosa. *Margaretha Adams*

1348. **Sarcoidosis. Preliminary Report on a Study of 350 Cases with Special Reference to Epidemiology**
M. MICHAEL, R. M. COLE, P. B. BEESON, and B. J. OLSON. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 403–407, Oct., 1950. 1 fig., 2 refs.

This paper gives a preliminary report on a study of 350 cases of sarcoidosis occurring among members of the U.S. Army during the late war. The geographical distribution of the birthplaces of the patients showed that there was a heavy preponderance of men born in the south-eastern states. Among white troops the case incidence was 22 per million in those from the south, compared with 4 per million in those from the north and west. The incidence in negro troops was 246 per million in those from the south, 16 in those from the north, and 61 in those from the west. For all areas the rate was 9 per million for whites and 178 per million for negroes. The comparatively very high incidence among negroes is related to the regional distribution of the disease, two-thirds of the negro troops coming from the south, where the rate was high, whereas two-thirds of the white troops were recruited from the north, where the rate was low. An interesting feature of the distribution is that the birthplaces of the patients were predominantly in rural areas. Positive tuberculin skin reactions were obtained in 46% of 56 patients who were born and spent most of their lives in urban areas, while only 23% of 107 patients from rural areas yielded a positive reaction. *W. J. Martin*

INDUSTRIAL MEDICINE

1349. **Treatment of "Seal Finger" with Aureomycin.** (Om spekkfinger behandling med aureomycin)
P. WAAGE. *Tidsskrift for den Norske Laegeforening* [*Tidsskr. norske Laegeforen.*] **70**, 679–681, Nov. 1, 1950. 12 refs.

The author reviews 24 cases of "seal finger" seen in Tromsö between April and June, 1950. This condition usually occurs in men engaged in seal catching, and occasionally also in those processing the catch in port, and is probably due to contagion from septic lesions occurring in the seals. It resembles erysipeloid, and the swelling is characterized by a cyanotic tinge. The infection may spread from the fingers to the hands and arms, and swelling of the regional lymph nodes was observed in one-third of the author's cases. The lesions are painful. None of the patients had fever when seen, but the erythrocyte sedimentation rate was greater than 30 mm. per hour in 4 cases.

Untreated cases may take 5 to 6 months to clear up, and there may be a residual ankylosis of the small joints. The author treated 20 cases with aureomycin in 12 to 16 doses of 250 mg. each, administered every 6 hours. The lesions became painless after 3 to 4 doses, the swelling was markedly reduced after 3 to 4 days, and the patient could return to work 1 to 2 weeks after completion of the course. *W. G. Harding*

1350. **Pneumokoniosis from Cereal Dusts.** (La pneumokoniose à poussières de céréales)
J. STEPHANOPOLI DE COMNÈNE and J. BESSON. *Archives des Maladies Professionnelles* [*Arch. Mal. prof.*] **11**, 459–470, 1950. 9 figs., 15 refs.

Six samples of dust from grains handled at the Marseilles docks contained 0·10 to 1·35% of free silica, and microscopical examination showed the dust to contain many sharp, hard particles of vegetable debris 30 to 35 μ long and 3 to 5 μ wide [there is an obvious misprint here in the original paper, where the dimensions are given in millimetres], large numbers of starch granules, and protein material, including bacteria and spores of fungi. The authors, who believe that the main noxious agent is the needle-like vegetable husk, exposed guinea-pigs to an atmosphere laden with the dust for short periods during 6 to 8 months, examined them radiologically at intervals, and later killed them. [No details

are given of the number of animals used or of the concentration of the dust inspired.] They claim to have observed radiological shadows in the lungs of these animals which they believe to have resulted from a combination of fibrosis and lobular collapse, and describe three morbid anatomical stages: (1) exudative bronchiolitis; (2) peribronchial thickening; and (3) peribronchial fibrosis, atelectasis, and thickening of the alveolar walls without any real alveolitis.

The criteria adopted by the authors for the radiological diagnosis of human pneumokoniosis were the presence of bilateral and symmetrical shadows that lessened from the hilum to the periphery of the lungs, of apical and basal emphysema, and of thickening of the diaphragmatic pleura. They recognize three stages: (1) reticulation with marked distortion of the hilar shadows; (2) reticulo-nodulation, frequently with pleural reactions, especially diaphragmatic; (3) bilateral pseudo-tumour formation. They examined 84 dockers and baggers clinically and radiologically and found abnormal shadows in the lungs of 21 of them (9 stage (1); 11 stage (2); 1 stage (3)). Soon after beginning their employment all these patients had had " grain fever ", which lasted a few days and was attended by cough and expectoration. During the next 5 to 20 years they had had frequent attacks of tracheo-bronchitis and gradually developed a chronic productive cough. By this time the radiological appearances were those of stage (1), but their general condition remained good. Progression to stage (2) appeared to be more rapid, and was accompanied by development of constant dyspnoea and some cyanosis. In none of the cases was evidence of tuberculosis found. Some men who had reached stage (2) slowly improved functionally when taken off dusty work, but the radiological appearances remained unchanged.

As preventive measures the authors advise the compulsory *x*-ray examination of all dock workers before enlistment and every 6 months thereafter, those showing evidence of bronchopulmonary disease or developing the appearances of stage (1) being taken off work involving exposure to dust, and the temporary suspension of men who develop intercurrent bronchopulmonary upsets. In addition, they advocate that dust be removed from the grain by cyclones in the aspirators used for unloading ships, or by exhaust ventilation where removal has to be performed manually.

[No deaths are reported, and it is impossible to determine from the paper whether the disability was severe in the few men who had any. The preventive measures advocated therefore seem rather heroic.]

H. E. Harding

1351. **Silicosis in Miners in Valais.** (La silicose des mineurs valaisans)
J. L. NICOD. *Mémoires de la Société Vaudoise des Sciences Naturelles* [*Mém. Soc. vaud. Sci. nat.*] **10**, 1–136, 1950. 27 figs., bibliography.

Although this report on the occurrence and nature of silicosis among the miners of Valais is based on a small number (179) of necropsies only, it is of value both because the investigations were thorough and because the working conditions in the mines and tunnels in this small area of Switzerland differ in some ways from those in countries from which large numbers of cases of silicosis have been reported. The workers are, in the main, only occasional miners, often working on the land during the summer and returning to mining or tunnelling during the dead season. The rocks are almost all highly siliceous, and the tunnels are generally 1,000 to 2,000 m. above sea level. Measures of dust-prevention have until recently been few or ineffective, partly because of ignorance, but largely because of local difficulties: only a few years ago workers in some of the tunnels were unable to see one another at a distance of more than one metre.

Among the cases studied, nodular silicosis was rather rare, the usual forms being either reticular (" *la tramite silicotique* ") or massive (*pseudo-tumorale*). The author has satisfied himself that this last type can, and often does, develop in the absence of any indication of tuberculosis and, further, that necrosis with subsequent cavitation may occur in silicotic masses, also without evidence of tuberculosis. [All cases were examined bacteriologically and histologically.] On the other hand, tuberculosis was a common complication in these cases, occurring in over 50%. Pleural adhesions were encountered only in cases where there had been bacterial infection (usually tuberculous) as well as silicosis. The author finds that reticulation is dangerous and disabling because the cuffing of vessels by histiocytes, and later by fibrous tissue, lowers the elasticity of the vessels and thus throws extra work on the right heart. Except in relation to the radiological picture, he does not appear to place much emphasis on emphysema. In several of the cases the period of exposure had been very short—in 36 it was less than 2 years, while one patient had worked in a tunnel for only 4 months in 1924, when he was 34 years old, and died 17 years later with massive silicosis and no trace of tuberculosis.

Reviewing the findings in this series, the author concludes that (1) the age of the miner when he is first exposed to dust plays no part in determining the development of pulmonary lesions; (2) the length of the period of exposure has no effect on the type of lesion; (3) stopping exposure to dust does not arrest the progressive evolution of the disease; and (4) silicosis may develop in a grave and fatal manner without the intervention of tuberculosis. *H. E. Harding*

1352. **Inhibition of Quartz-induced Fibrosis of the Liver by Aluminium**
C. V. HARRISON, B. M. WRIGHT, and E. J. KING. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 443–444, July, 1950. 18 figs., 4 refs.

Experimental hepatic fibrosis was induced in rabbits by the intravenous injection of quartz dust. It was found that when powdered aluminium or aluminium hydroxide was administered together with the quartz dust the production of fibrosis was greatly retarded. This study confirms the earlier work of Gardiner *et al.*, (*J. industr. Hyg.*, 1944, **26**, 211), and suggests that aluminium probably hinders the fibrogenic action of silica by rendering it less soluble. *G. J. Cunningham*

Genetics

1353. **The Combination of Blood Groups in a Sample of 475 People in a London Hospital**
D. BERTINSHAW, S. D. LAWLER, H. A. HOLT, B. H. KIRMAN, and R. R. RACE. *Annals of Eugenics* [*Ann. Eugen., Camb.*] **15**, 234–242, Oct., 1950. 1 ref.

1354. **The Inheritance of the Lutheran Blood Groups in Forty-seven English Families**
S. D. LAWLER. *Annals of Eugenics* [*Ann. Eugen., Camb.*] **15**, 255–257, Oct., 1950. 5 refs.

The anti-Lu^a serum Egl (of Ikin) can be used satisfactorily at room temperature with a 2% suspension of erythrocytes in saline for testing cells of all ABO groups when diluted with an equal volume of A_1 B-secretor saliva. Specimens of blood from members of 47 English families were tested for the presence of the Lu^a antigen. Of 34 Lu(a−) by Lu(a−) matings all the 77 children were Lu(a−). Of 12 Lu(a−) by Lu(a+) matings there were 12 children who were Lu(a+) and 5 who were Lu(a−). Of a single Lu(a+) by Lu(a+) mating there were 2 Lu(a+) and 1 Lu(a−) children. Thus the Lu^a antigen is inherited as a Mendelian dominant character. In the families of the mating Lu(a—) by Lu(a+) it was found that the Lu^a gene segregates independently of the ABO, MNS, Rh, Lewis, and Kell systems.

The gene frequencies of Lu^a and Lu^b in England were estimated by combining the results of the three large surveys so far published. Assuming that the Lu^a antigen is inherited as a dominant, the gene frequency of Lu^a is 0·039 and that of Lu^b 0·961. *C. O. Carter*

1355. **Inheritance of the Rh Blood Groups: 150 Families Tested with Anti-C–c–C^w–D–E and Anti-e**
S. D. LAWLER, D. BERTINSHAW, R. SANGER, and R. R. RACE. *Annals of Eugenics* [*Ann. Eugen., Camb.*] **15**, 258–270, Oct., 1950. 10 refs.

Blood samples from 150 English families were tested with anti-C–c–C^w–D–E and anti-e sera. (A further 30 English families of which details have already been published (Sanger *et al.*, *Heredity*, 1948, **2**, 131) are included in the analysis.) The three allelomorphic antigens, Cc, Ee, and Dd were first taken separately and the expected proportions of the various mating types and their children were calculated from the known gene frequencies of the antigens. In the case of Dd, only the phenotypes D and dd are distinct in the absence of anti-d, and the expectations were obtained by appropriate pooling of the genotypes. The proportions observed agreed well with those expected. Secondly, the proportions of the various phenotype matings expected, defined by the use of anti-C–c–D and anti-E sera only, were calculated and these again were found to agree well with the proportions observed. The calculation for the expected issue of the phenotype matings involving R_1 r made by Race and Sanger was applied and found to fit well with the observed phenotypes of the children.

It is thus confirmed that the antigens C and c, E and e, D and d are inherited as Mendelian characters and in threes—C or c, D or d, and E or e. *C. O. Carter*

1356. **Rhesus Type D^u**
P. H. RENTON and F. STRATTON. *Annals of Eugenics* [*Ann. Eugen., Camb.*] **15**, 189–209, Oct., 1950. 2 figs., 14 refs.

Samples of erythrocytes containing modified forms of the D antigen were investigated. These were obtained from donors found to be R′ (Cde) or R″ (cdE) on routine testing, and from donors previously noted as giving weak or anomalous results with anti-D sera. Those erythrocytes reacting with a strong anti-C+D agglutinating serum but weakly or not at all with an anti-E, and those reacting with the incomplete, but not with the agglutinating, anti-D sera, were considered to be examples of D^u and tested further with a series of 49 random agglutinating sera and 12 incomplete sera selected for high strength. A number of erythrocytes containing ordinary D and d were also tested as controls.

It was found that various stypes of D^u, reacting with various proportions of the sera used, could be distinguished. In general the results suggested a quantitive variation in the amount of D^u antigen in the erythrocytes of the various samples tested, but there were significant exceptions. High-grade D^u cells gave positive results with a proportion of the agglutinating sera, gave positive Coombs-test reactions with a proportion of incomplete sera, and gave negative results in the albumin test, with occasional exceptions. Low-grade D^u cells gave negative results with agglutinating sera or weak positive results with a few of those of highest titre, gave positive Coombs-test reactions with a proportion of incomplete sera, and gave negative albumin reactions with incomplete sera. With some sera and cells the Coombs test was positive and the albumin test negative, while with others the Coombs test was negative and the albumin positive. About one-third of a random sample of 209 sera containing anti-D antibodies reacted with fairly high-grade erythrocytes of type R_2^{u}, (cD^{u}E).

The distinction between D^u and d is effected with specially strong anti-D agglutinating sera or with a series of incomplete sera using the Coombs test; several sera must be used. The distinction between D^u and D can be made roughly with the albumin test, using several strong incomplete sera, but to do this accurately it would be necessary to set up a chart comparing the reactions of various sera with various types of cell. The risk of overlooking D^u in supposedly Rh-negative blood can be minimized by using anti-C and anti-E sera. Agglutinating sera for use as Rh-testing sera should be tested with a series of Rh-positive cells, including high-grade D^u

cells. In investigating transfusion reactions and cases of haemolytic disease both the Coombs and albumin tests must be used. The gene frequency of D^u is estimated as 0·444‰, but there is reason to suppose that this estimate is too low. The inheritance of D^u was traced in 10 families and it was found to behave as an allele at the D–d locus. The reactions with anti-D sera of cells with D^u within a family are much alike.

C. O. Carter

1357. **Genetics of Convergent Strabismus.** [In English] G. DAHLBERG and W. NORDLÖW. *Acta Genetica et Statistica Medica* [*Acta genet., Basel*] **2**, 1–14, 1951. 11 refs.

1358. **Congenital Total Colour Blindness associated with Otosclerosis**

A. G. MACGREGOR and R. HARRISON. *Annals of Eugenics* [*Ann. Eugen., Camb.*] **15**, 219–233, Oct., 1950. 1 fig., 47 refs.

The pedigree of a family is described in which the index case was a woman who was totally colour-blind, had bilateral otosclerotic deafness, and was hypertensive. The authors examined personally 46 of her living relatives, including all her sibs, and obtained information about 71 others. Of the woman's 10 sibs, 1 brother had total colour-blindness, otosclerotic deafness, and hypertension, a twin sister (not identical) and another sister had total colour-blindness and otosclerotic deafness, 2 sisters had otosclerotic deafness and hypertension, 4 brothers had otosclerotic deafness alone, and one sister was normal. The woman's mother was reported to have had otosclerotic deafness and hypertension, and of the mother's 3 sibs 1 was found to have hypertension and 1 was reported to have otosclerotic deafness. The mother's mother was also reported to have had otosclerotic deafness, and of her 4 children by another marriage 1 was found to have hypertension and another reported to have had otosclerotic deafness. None of the 6 children of the individuals with total colour-blindness was himself affected. The criteria for the diagnosis of total colour-blindness were complete inability to interpret any but the first Isahara test plate, presence of the associated stigmata of photophobia and poor central vision, and characteristic findings on testing field of vision, dark adaptation, and spectral visibility. Otosclerosis was diagnosed when deafness was found to be gradual in onset after adolescence and was not preceded by suppurative aural disease. All the affected individuals examined gave a negative response to Rinné's test. Essential hypertension was diagnosed when the diastolic pressure was greater than 100 mm. Hg in the absence of a history of renal disease or pregnancy toxaemia.

The manner of inheritance in this family is consistent with the view that total colour-blindness is inherited as a Mendelian recessive, and hypertension and otosclerotic deafness as Mendelian dominants. The pedigree provides good evidence against a close linkage between the genes for hypertension and otosclerosis, or for hypertension and congenital total colour-blindness, but provides no evidence against a linkage of the genes for otosclerosis and total colour-blindness. *C. O. Carter*

1359. **A Maternal Influence on the Incorporation of Methionine into Liver Protein**

R. J. RUTMAN. *Science* [*Science*] **112**, 252, Sept. 1, 1950. 3 refs.

Liver slices from rats of two different highly-inbred strains were found to incorporate DL-methionine labelled with radioactive sulphur at different rates, and the rats of the strain with the higher rate of methionine incorporation grew more rapidly than the others. Young litters from each strain were interchanged and fostered by mothers of the other strain. After weaning and growth on a standard diet until a weight of 100 g. was reached, the rats were killed and the methionine exchange of slices of their livers compared with control slices. Rats of the strain with a lower rate of methionine incorporation grew more rapidly, and slices of their livers incorporated methionine at a higher rate, when nursed by foster-mothers of the other strain than by their own mothers. No reciprocal depression of methionine incorporation or of growth was observed. The question is posed as to whether genetically-determined differences in the incorporation of amino-acids may play some role in the influence of milk on the growth of young mammals.

H. Kalmus

1360. **The Familial Distribution of Diabetes Mellitus: a Study of the Relatives of 1241 Diabetic Propositi**

H. HARRIS. *Annals of Eugenics* [*Ann. Eugen., Camb.*] **15**, 95–119, March, 1950. 1 fig., 19 refs.

Detailed family information obtained from 1,241 diabetic subjects was analysed. Hereditary influences are much more strongly indicated in cases of early onset; thus about 7% of the sibs of those developing diabetes before the age of 30 may be expected to be similarly affected before the age of 40, whereas the figure is only about 1·3% for the sibs of those developing the disease after 30. The expectation among children of diabetic subjects is much lower than in sibs, as would be expected if the genes concerned are recessive, which is very generally accepted to be the case. It is possible that cases of late onset may be heterozygous for a gene which, in double dose, produces cases of early onset.

J. A. Fraser Roberts

1361. **Hereditary Factors in Peptic Ulcer**

R. DOLL and J. BUCH. *Annals of Eugenics* [*Ann. Eugen., Camb.*] **15**, 135–146, March, 1950. 12 refs.

The incidence of peptic ulcer in the living sibs and parents of 309 patients with peptic ulcer was investigated and compared with that in a control population. The incidence among brothers and sisters was rather more than double that to be expected on the basis of the control population, and the incidence among fathers was also significantly increased, but the number of available mothers was insufficient for analysis. It is suggested that it is reasonable to conclude that hereditary factors are of importance in the production of peptic ulcers. Familial tendencies were stronger in cases of duodenal than of gastric ulcer, and also where the onset was early. There was a strong tendency for sibs to develop ulcers at the same site. *J. A. Fraser Roberts*

Physiology and Biochemistry

1362. **Studies on the Antigens of Human Red Cells. I. The Separation from Human Erythrocytes of a Water Soluble Fraction Containing the Rh, A, and B Factors**
M. MOSKOWITZ, W. B. DANDLIKER, M. CALVIN, and R. S. EVANS. *Journal of Immunology* [*J. Immunol.*] **65**, 383–392, Oct., 1950. 9 refs.

Elinin, a lipoprotein fraction of the stroma of erythrocytes with which are associated the Rh, A, and B factors, may be extracted from erythrocytes in the following way: Citrated human blood is centrifuged to obtain erythrocytes, which are then haemolysed with ten times their volume of distilled water. The haemolysate is passed through a Sharples centrifuge and the sediment freeze-dried: the freeze-dried material, after prolonged extraction with ether in a Soxhlet apparatus, is suspended in water, adjusted to *p*H 9 to dissolve it, and clarified by centrifugation. The salt concentration of the supernatant is then raised to 0·15 M by the addition of 5 M sodium chloride solution, keeping the *p*H near 9 throughout; the material is then centrifuged at 10^5 "g" for half an hour; the sediment is resuspended in water and the process repeated to yield as sediment about 1 g. of elinin per 600 ml. packed erythrocytes. Elinin in 1% solution is clear, transparent, and yellowish-brown, but scatters light considerably. Such solutions show streaming birefringence at *p*H 9, this diminishing as the *p*H is lowered, and disappearing at *p*H 7. In more acid solutions turbidity develops and at *p*H 5·4 to 5·2 a floccular precipitate forms, which does not dissolve when the *p*H is adjusted to 2 or 9. Electrolytes in concentrations as low as μ=0·01 reduce the birefringence and produce turbidity in the solutions. The particle weight of elinin is 40,000,000. Although elinin derived from Rh-positive A erythrocytes inhibits the agglutination of Rh or A cells by the homologous antisera, it is not itself antigenic in rabbits. This Rh activity can be destroyed by heating to 56° C. for 5 minutes, or by extraction with ether, or by ageing, or by treatment for 5 minutes with crystalline trypsin; the A activity is, however, far more stable.

From the supernatant from the haemolysate another protein (S protein) may be obtained as follows: The supernatant is centrifuged until water-clear and the clear liquid adjusted to *p*H 6·5 with 1 M hydrochloric acid. The floccular precipitate formed is washed several times with water and constitutes S protein. It differs from elinin in having a lower molecular weight, in being insoluble at *p*H 6·5 in water (though soluble at this *p*H in 0·15 M NaCl), and in having no Rh, A, or B activity.

C. L. Oakley

1363. **Observations on the Genesis of the Electrocardiogram**
R. H. ROSENMAN. *American Heart Journal* [*Amer. Heart J.*] **40**, 522–530, Oct., 1950. 2 figs., 27 refs.

1364. **A Discrepancy between Renal Extractions and Urinary Excretion of Various Substances (*para*-Aminohippurate, Mannitol, Creatinine, Thiosulphate) in Man**
F. C. REUBI, H. A. SCHROEDER, P. H. FUTCHER, and C. REUBI. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 63–76, Aug., 1950. 2 figs., 18 refs.

Discrepancies observed between the values for renal plasma flow determined by renal venous catheterization and those determined by clearance methods suggest that the latter must be interpreted with caution. In order to study the constancy of the discrepancies and the effect of certain drugs, experiments were carried out on 9 subjects, 6 of whom suffered from essential hypertension, at Washington University and Barnes Hospital, St. Louis. The discrepancy could in every case be modified by the injection of adrenaline or histamine, but not in a uniform manner. The possible sources of these discrepancies are discussed and include differences in extraction rates of the two kidneys (catheterization was performed on the right side only), intra-renal conjugation of the test substances used, partial removal of these substances by the lymphatics, changes in urine and plasma blanks; changes in erythrocyte permeability, and analytical difficulties.

[This appears to be an important paper in view of the doubt it casts on the reliability of accepted research procedures. It should be read in the original by those interested.] *A. T. Macqueen*

1365. **The Development of the Active State of Muscle during the Latent Period**
A. V. HILL. *Proceedings of the Royal Society. B.* [*Proc. roy. Soc. B*] **137**, 320–329, Oct. 31, 1950. 7 figs., 14 refs.

The author has recently reported (*Proc. roy. Soc. B.*, 1949, **136**, 399) investigations into the mechanical condition of an active muscle by applying a rapid stretch at various moments after a maximal shock. Working with frog and toad muscles, he found that at the end of the latent period there was an apparently abrupt change of state, the contractile component of the muscle becoming capable of bearing a considerable load. In the present experiments the author used the extensor tibialis muscle of the tortoise, a much slower-acting muscle. At 0° C. it has a latent period of 60 to 70 milliseconds, and the twitch tension reaches its maximum in 3 to 4 seconds. The heat of activation starts at about 60% of the latent period after the shock. It was found that at about 50% of the latent period after the shock there began to develop a state of enhanced rigidity of the muscle (increased resistance to stretch), which reached its maximum within a few hundredths of the time to the isometric twitch-tension maximum. This state gradually disappeared as relaxation of the muscle set in. It has been reported that frog's muscle shows a very small "latency relaxation" and an increase in transparency at

about half-way through the latent period. The author suggests these are physical signs of the altered mechanical condition of the muscle (increased rigidity), while the heat of activation can be looked upon as a sign of the chemical changes that bring about the mechanical and physical alterations. *P. Mestitz*

1366. **Results of Four Years' Medical Surveillance of the Flying Personnel of a Large Commercial Air-line.** (Quatre années de surveillance médicale du personnel navigant d'une importante société de navigation aérienne) A. ALLARD. *Bruxelles-Médical* [*Brux.-méd.*] **30**, 1682–1873, Sept. 3, 1950.

The 6-monthly and twice-monthly medical examinations to which flying personnel of the Sabena airline are subjected are described. The results of medical examinations over a period of 4 years (1946–9) of pilots, navigators, wireless operators, flight mechanics, stewards, and air hostesses are presented and compared. Their excellent health is commented on. Differentiation is in some cases made between subjects habitually flying in unpressurized and in pressurized aircraft. Pressurization has no unfavourable effect and diminishes fatigue. In 65% of examinations of air hostesses an abnormal erythrocyte sedimentation rate was found. This is regarded as being associated with the more prolonged and profuse menstruation of which many air hostesses complained. *T. C. D. Whiteside*

RESPIRATORY SYSTEM

1367. **Influence of O_2 Content of Inspired Air on Total Lung Volume**
E. PEYSER, A. SASS-KORTSÁK, and F. VERZÁR. *American Journal of Physiology* [*Amer. J. Physiol.*] **163**, 111–117, Oct., 1950. 9 figs., 12 refs.

By means of body plethysmograph readings it was found that in cats and rabbits under urethane anaesthesia oxygen-poor mixtures (5 to 8% O_2) increase the volume of the lungs. The addition of carbon dioxide (2 to 10%) to the inspired air had no such effect. There was no correlation between increase in total lung volume and increase in respiratory rate, tidal air, or respiratory minute volume. The lung volume was found to increase as the oxygen content of the inspired air decreased.
A. Schweitzer

1368. **Role of Pulmonary Proprioceptive Reflexes in Suppression of Spontaneous Breathing during Electrophrenic Respiration**
P. O. CHATFIELD and S. J. SARNOFF. *American Journal of Physiology* [*Amer. J. Physiol.*] **163**, 118–124, Oct., 1950. 5 figs., 10 refs.

In anaesthetized dogs the right phrenic nerve was rhythmically stimulated and action potentials were recorded from the left, unstimulated, leaf of the diaphragm. Inhibition of spontaneous respiration was not observed when the rate of artificial breathing was too slow, but could be produced by increasing the artificial breathing rate. Lengthening the duration of inspiration in the artificial rhythm, without changing its rate or depth, abolished spontaneous respiration. Section of the vagi abolished the inhibition of spontaneous breathing during electrophrenic respiration. The facility with which spontaneous breathing could be suppressed was decreased by inducing hypercapnia. During electrophrenic respiration action potentials from the intercostal muscles were inhibited in the same way as were those from the diaphragm. It is concluded that suppression of spontaneous breathing during electrophrenic respiration is due to inhibitory vagal impulses acting on the respiratory centre. *A. Schweitzer*

1369. **Efficacy of Artificial Respiration**
E. ASMUSSEN and M. NIELSEN. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 95–102, Aug., 1950. 3 figs., 10 refs.

In this paper from the University of Copenhagen, the authors describe a method of evaluating the several different methods of artificial respiration in the living subject without the need for anaesthetization or interference with the normal mechanism of chemical control of respiration. It consists in measuring the changes in supplemental and residual air induced by the method of artificial respiration used, the subject's lungs being connected to a spirometer so as to form a closed circuit.

Investigations were carried out on 6 males and 5 females, aged 21 to 46, who were trained to relax completely during the experiments. Tidal air during artificial respiration by the Schafer method was found to be 180 c.cm., by the Holger Nielsen method, 450 c.cm., and by Eve's method, 540 c.cm. They conclude that the Schafer method is incapable of giving adequate ventilation. Of the other two, the Holger Nielsen method has an advantage over Eve's method in that it can be carried out by one man. *A. T. Macqueen*

1370. **The Pressures Developed in Abdomen and Thorax during the Flack Tests**
J. N. MILLS. *Journal of Physiology* [*J. Physiol., Lond.*] **111**, 368–375, Oct. 16, 1950. 4 figs., 14 refs.

A series of experiments to test the validity of the Flack tests of circulatory and respiratory efficiency were carried out on the author, supine on a couch, optical manometers being used to measure the pressures developed in the abdomen and lungs. In the test involving measurement of maximum expiratory pressure against a mercury column it was found that the intra-abdominal pressure was higher than the mouth pressure if the initial chest volume was small, while the reverse was the case if the initial chest volume was large. During the second Flack test, involving maintenance of a mercury column at 40 mm. by expiratory effort, both intrathoracic and intra-abdominal pressures fell to low values during the effort, while the mouth pressure remained high. This was presumably due to closure of the glottis. The decrease in the thoracic pressure during the expiratory effort in the second test makes this test especially unreliable as an index of the state of the subject's circulation. It still remains to be proved that either of the tests gives information of any constant significance at all. *P. Mestitz*

1371. **The Nature of the Limitation of Maximal Inspiratory and Expiratory Efforts**
J. N. MILLS. *Journal of Physiology* [*J. Physiol., Lond.*] **111**, 376–381, Oct. 16, 1950. 3 figs., 4 refs.

In order to determine the cause of variation in successive determinations of the vital capacity, which is mainly due to variability of the inspiratory end-point, the mode of limitation of maximal respiratory movements was investigated by measuring the intra-abdominal pressure, by recording action potentials from muscles of the abdominal wall, and by observation of the glottis, in 15 healthy subjects in the supine position. In most of the subjects examined, maximal inspiration was terminated by contraction of the abdominal muscles and involuntary closure of the glottis. *P. Mestitz*

1372. **Studies of Lung Capacities and Intrapulmonary Mixing: Normal Lung Capacities**
J. B. BATEMAN. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 133–142, Sept., 1950. 3 figs., 6 refs.

1373. **Studies of Lung Volume and Intrapulmonary Mixing. Nitrogen Clearance Curves: Apparent Respiratory Dead Space and its Significance**
J. B. BATEMAN. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 143–160, Sept., 1950. 4 figs., 21 refs.

NUTRITION AND DIGESTION

1374. **Perspiration as a Factor Influencing the Requirements for Calcium and Iron**
F. A. JOHNSTON, T. J. MCMILLAN, and E. R. EVANS. *Journal of Nutrition* [*J. Nutrit.*] **42**, 285–296, Oct. 10, 1950. 8 refs.

In experiments at Cornell University perspiration was collected from 4 normal young women, each of whom first scrubbed herself in a bath of hot, soapy water for about half an hour, was then rinsed with hot distilled water and patted dry with towels, and then sat in the sweating chamber for approximately one hour so that the perspiration from all parts of the body (except from the scalp, which was kept wrapped in a cheese cloth) dripped into enamel pans. The subjects were then thoroughly rinsed with warm distilled water. The temperature readings in the hot chamber were 97° F. (36° C.) dry bulb and 93° F. (34° C.) wet bulb. Care was taken to prevent contamination from outside. The procedure was carried out on 4 occasions with each subject. The collected perspiration and the ultimate rinsings were filtered and analysed for iron (after ashing) and for calcium.

The mean loss of body weight per hour for all subjects during the collection periods was 10·9 oz. (308 g.). The mean loss of iron for all subjects was 0·25 mg. per kg. of body weight and 0·075 mg. per hour. The mean loss of calcium for all subjects was 29 mg. per kg. body weight and 8·5 mg. per hour. The results show that the loss of iron in perspiration is small. It is considered, however, that these losses of calcium and iron are " such as to indicate that the intake of the average woman engaging in average activity under average conditions of temperature and humidity must be increased a little to cover them." *Joseph Parness*

1375. **Investigation of Hepatic Function by Clearance Techniques**
A. E. LEWIS. *American Journal of Physiology* [*Amer. J. Physiol.*] **163**, 54–61, Oct., 1950. 4 figs., 9 refs.

1376. **A Quantitative Study of the Gastric Secretory Response to Sham Feeding in a Human Subject**
H. D. JANOWITZ, F. HOLLANDER, D. ORRINGER, M. H. LEVY, A. WINKELSTEIN, M. R. KAUFMAN, and S. G. MARGOLIN. *Gastroenterology* [*Gastroenterology*] **16**, 104–116, Sept., 1950. 3 figs., 13 refs.

The cephalic phase of gastric secretion cannot readily be studied in isolation, and there is little information on this aspect of digestion. A young woman with traumatic high oesophageal stenosis and a gastrostomy was therefore subjected to sham feeding with various meals and the gastric secretions and motility investigated. Since she was accustomed to eat her meals in a normal fashion and then regurgitate them before each intragastric feed, the experiment introduced no unusual activities.

After a sham meal of her own choosing, the gastric response was considerable, easily surpassing that provoked by insulin hypoglycaemia or histamine. In twelve feeds the average total volume of gastric secretion was 212 ml. (range, 154 to 361 ml.), containing 16·14 (9·8 to 36·0) mEq. of hydrochloric acid and 53,000 (28,000 to 80,000) units of pepsin. Sham feeding with a routine hospital meal produced a much smaller volume, while gruel provoked no response at all.

True hunger contractions were seldom recorded, in contrast to the findings in many animal experiments.
Richard Terry

1377 (*a*). **Release of Gastrin in Response to Bathing the Pyloric Mucosa with Acetylcholine**
C. R. ROBERTSON, K. LANGLOIS, C. G. MARTIN, G. SLEZAK, and M. I. GROSSMAN. *American Journal of Physiology* [*Amer. J. Physiol.*] **163**, 27–33, Oct., 1950. 1 fig., 22 refs.

In experiments performed at the University of Illinois on dogs provided with an isolated pyloric pouch and a vagotomized fundal pouch, irrigation of the pylorus for 30 minutes with 50 ml. of 0·5% acetylcholine bromide solution in saline caused a marked increase in acid gastric secretion in the fundal pouch. Subcutaneous injection of a similar amount of the drug did not stimulate gastric secretion. The juice secreted was very low in pepsin content, indicating that the humoral agent concerned was gastrin and not acetylcholine itself. Irrigation of the pyloric pouch with 0·5% nicotine solution did not stimulate secretion from the fundal pouch. The effect of acetylcholine was abolished by atropine.

[These experiments provide convincing evidence for the existence of a gastric hormone in the pyloric region and indicate that its release is under nervous control.]
R. A. Gregory

1377 (*b*). **Effect of Surgical Extirpation of Pyloric Portion of the Stomach on Response of Fundic Glands to Histamine and Urecholine in Dogs**
K. J. LANGLOIS and M. I. GROSSMAN. *American Journal of Physiology* [*Amer. J. Physiol.*] **163**, 38–40, Oct., 1950. 2 refs.

In the work reported here the hypothesis put forward in the authors' previous paper (see Abstract 1377 (*a*)), that cholinergic stimuli release gastrin from the pyloric mucosa, was studied further in dogs by determining the effect of surgical removal of the pyloric pouch on the acid response to injection of " urecholine " of a vagotomized fundal pouch. As a control the response of the fundal pouch to the injection of histamine before and after pylorectomy was determined, as also was the response to a combination of histamine and urecholine. After pylorectomy the response of the fundal pouch to histamine was unaltered, but that to urecholine fell markedly (by 80 to 90%), supporting the earlier conclusion that cholinergic drugs produce acid secretion by liberating gastrin from the pyloric mucosa. The response to the two drugs together was unaltered. The suggestion is made that cholinergic drugs, although almost ineffective as direct stimulants of the parietal cell, sensitize it to other stimuli. *R. A. Gregory*

1378. **Chemical Changes Produced in Isotonic Solutions of Sodium Sulfate and Sodium Chloride by the Small Intestine of the Dog**
G. R. BUCHER, C. E. ANDERSON, and C. S. ROBINSON. *American Journal of Physiology* [*Amer. J. Physiol.*] **163**, 1–13, Oct., 1950. 19 refs.

In the experiments reported in this paper isotonic solutions of sodium sulphate (202 mEq. per litre) were introduced into isolated jejunal and ileal loops in dogs and a study made of the changes which subsequently occurred in the volume, total cation, sulphate, chloride, bicarbonate, and ammonia content and the *p*H of the contents of the loop. Sodium chloride was readily absorbed from both upper and lower intestinal loops, especially the latter, and in both loops the *p*H and bicarbonate content rose during absorption, indicating that more Cl^- than Na^+ had left the loop and that the excess had been replaced by HCO_3^-. This effect was also greater in the lower intestinal loop. In jejunal loops the total cation content increased during absorption, whereas in ileal loops there was no change. [Visscher and Roepke (*Amer. J. Physiol.*, 1943, **144**, 468) found that isotonic solutions of sodium chloride (153 to 160 mEq. per litre) became hypotonic (143 mEq. per litre) during absorption from ileal loops. The present authors state that such a solution is absorbed from such loops without further change.] During the absorption of the sodium sulphate solution from jejunal loops, fluid entered the intestine and the fluid became more acid than during the absorption of sodium chloride solution. Quantitative differences were observed as between upper and lower intestinal loops and between initial and subsequent determinations on the same loop. Evidence of an exchange of chloride and bicarbonate ions was found as with the chloride solutions. *R. A. Gregory*

1379. **The Concentration of Cholesterol in the Blood Serum of Normal Man and its Relation to Age**
A. KEYS, O. MICKELSEN, E. O. MILLER, E. R. HAYES, and R. L. TODD. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1347–1353, Oct., 1950. 15 refs.

At the University of Minnesota the authors made 5,000 estimations of serum total cholesterol concentration, both by the Schoenheimer–Sperry and by the Bloor method, on the sera of 2,056 individuals between 17 and 78 years of age. No significant difference of concentration was observed whether the blood was collected when the subject was fasting and at rest or at rest only, and no significant difference was found between the results of the two estimations, which were carried out in different laboratories. There was an increase in the mean serum cholesterol level averaging 2·29 mg. per 100 ml. between the ages of 17 and 75 years. For subjects between 17 and 30 years (there being no females in the series outside this age group) the serum cholesterol content of the two sexes did not differ significantly. There was a pronounced curvilinear relationship between age and serum total cholesterol concentration, which reached its maximum in the sixth decade after which it declined in old age.

[The close agreement between the results of estimations by the Sperry–Schoenheimer and the Bloor techniques reported in this paper may occasion some surprise.]
Walter H. H. Merivale

1380. **The Feeding of School-children**
F. ROBERTS. *Lancet* [*Lancet*] **2**, 434–438, Sept. 30, 1950. 7 figs.

In a secondary modern school in Cambridgeshire not more than 27% of the children could be made to drink milk despite every inducement, and the food consumed at the school dinner fell short by about 150 Calories of the 1,000 Calories recommended by the Ministry of Education. The state of the stomach at different times of the day was therefore investigated by radiography after a small barium meal.

Some children normally took milk and a substantial packed lunch at the morning break at 10.35 a.m.; this intake might amount to 370 Calories. If a child then ate, at 12.30 p.m., the dinner recommended by the Ministry, he would be consuming 1,370 Calories within 2 hours. This is shown to be an impossible feat: the children who had taken milk, with or without lunch, 2 hours previously had a considerable quantity of food in the stomach at dinner-time and were in general not hungry. Further, whether the milk had been taken or not, the children failed to consume a dinner of 788 Calories. If milk was taken at 9·45 a.m., the stomach was empty at dinner-time 3 hours later. It is concluded that milk should be taken some 3 hours before dinner and that a packed lunch at the mid-morning break is unnecessary.

[This valuable study is marred by errors and loose statements: for instance, the author states that " children, boys especially, always have eaten and always will eat anything at any time of the day ", which is contrary to the main theme of his paper; child No. 8 is stated to have breakfasted on an egg and fried potatoes, but six lines lower he or she (for ages, and sometimes sexes,

are not given) is said to have had bacon and one piece of bread and butter; fig. 6 illustrates the stomachs of 4 children, but according to the text only 3 boys were included.] *H. M. Sinclair*

1381. **School Lunches: their Nutritive Value and Relation to the Health and Diet of Children**
M. L. HATHAWAY, F. L. MEYER, and S. F. ADELSON. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **40**, 1096–1100, Sept., 1950.

This investigation falls into three parts: (1) an assessment of the nutritive value of school lunches; (2) a study of the effect of partaking of school lunches on the nutritional status of children; (3) a comparison of the nutritive value of the diets of children taking, and of those not taking, school lunches.

In 15 schools from 7 States a total of 70 meals was analysed. The nutrient content of these varied enormously. Whether or not a child took milk made an appreciable difference, as would be expected, to the amounts of protein, riboflavin, and calcium consumed. It is considered that the school lunch should provide one-third of the amounts recommended for daily consumption by the National Research Council; on this basis, of the 70 meals only 8 were adequate in calories, 58 in protein, 32 in ascorbic acid, and 10 in aneurin. [Since the meals as served were analysed without allowing for plate waste, or for the second helpings which were usually available, these conclusions are open to suspicion.]

Haemoglobin value and serum ascorbic-acid level were measured in children attending two schools in one locality. School lunches were available in one of the schools throughout the 2 years of study, while in the other school they were available only in the second year. There was no difference between the haemoglobin values in children who had the lunch and those who did not. On the other hand, the proportion of children with a high concentration of ascorbic acid in serum was lowest in those who had no school lunch during the 2 years, was greater in those who had had it for one year, and was greatest in those who had had it for the 2 years.

Surveys of the total food consumed by some of the children for 7 days were made from records kept by their mothers. Those taking the school lunch had a better intake of nutrients, especially of calcium and vitamins A and C, than those who did not. [The number of children in this survey and the details of consumption are not given.] *J. Yudkin*

ENDOCRINE GLANDS

1382. **Role of the Thyroid in Metabolic Responses to a Cold Environment**
E. A. SELLERS and S. S. YOU. *American Journal of Physiology* [*Amer. J. Physiol.*] **163**, 81–91, Oct., 1950. 4 figs., 10 refs.

When adult white rats were exposed to cold (1·5° ± 1° C.) in experiments carried out at the University of Toronto, the metabolic rate, as indicated by oxygen consumption, increased immediately to about double the normal value in the first day, and more slowly thereafter to a level of 2·7 times normal after 8 days. In prolonged experiments (3 months) the values showed a tendency to decline. The metabolic rate determined at 30° C., the animals being removed from the cold room 30 minutes beforehand, rose gradually to 17% above normal in 8 days and ultimately reached a level 30 to 50% above normal in 2 weeks. Thereafter no further increase occurred. The average colonic temperature of rats in the cold room was 37·7° C., that of controls at 30° C. being 37·1° C., the difference being statistically significant ($P<0·01$). The metabolic rate measured at 1·5° C. was greatly reduced when the rats were anaesthetized with sodium pentobarbitone, indicating that a large part of the increased heat production in conscious rats at this temperature was due to muscular activity. The effect of anaesthesia on the metabolic rate measured at 30° C. was far less. In rats deprived of thyroid activity by thyroidectomy or administration of propylthiouracil and receiving 2·5 to 5 μg. of thyroxine daily a marked increase in the metabolic rate, as measured at 30° C., occurred during exposure to cold, indicating that the increased metabolic rate in cold was not dependent on increased thyroid activity.

After thyroidectomy, rats failed to survive more than a few days at 1·5° C., although those previously acclimatized to this temperature lived slightly longer than unacclimatized animals. Their metabolic rate as measured at 1·5° C. was raised, but the metabolic rate as measured at 30° C. approached the low values obtained in rats deprived of thyroid activity and living at room temperature. An increase in pituitary thyrotrophic activity was observed after 2 weeks' exposure to cold and was sustained for at least 3 months. It was unaffected by the administration of sodium iodide. It is suggested that the increase in metabolic rate, as measured at 30° C., on exposure to cold is not due to a hyperthyroid state, but does depend on the presence of the thyroid. *R. A. Gregory*

1383. **Excretion of Administered Radio-calcium following Thyroparathyroidectomy, or Bilateral Nephrectomy, and the Injection of Parathyroid Extract**
W. R. TWEEDY, M. V. L'HEUREUX, and E. M. ZORN. *Endocrinology* [*Endocrinology*] **47**, 219–227, Oct., 1950. 16 refs.

The influence of the parathyroids and kidneys on the excretion of calcium has been studied by the authors at Loyola University, Chicago, using Sprague–Dawley rats kept on a stock diet of adequate calcium and phosphorus content (only one rat showed signs of tetany in the course of the work). Radioactive calcium was administered subcutaneously or intraperitoneally, and its excretion observed over an 18-hour period. (The experimental methods are described in a previous paper by the same authors (*Proc. Soc. exp. Biol., N.Y.*, 1949, **71**, 729).)

Thyroparathyroidectomy caused no consistent change in the rate of renal excretion of radiocalcium, but faecal excretion was temporarily diminished and returned to normal only 24 to 40 days after operation. The serum

calcium level in the experimental animals 24 hours after thyroparathyroidectomy and 18 hours after the administration of radiocalcium was lower than that of the controls, and tissue analysis showed that the calcium retention was largely extraskeletal. Thyroparathyroidectomized rats treated with parathyroid extract excreted no more calcium than without the hormone, but their serum calcium level was higher and tissue analysis indicated an accumulation of calcium in the kidneys. The authors, on the basis of previous work, consider this to be the result of phosphorus retention by the kidneys. The faecal calcium output of totally nephrectomized rats was diminished and was not restored to normal by administration of parathyroid. Previous work showing that radiophosphorus is retained by the tissues of nephrectomized animals suggests that the calcium is immobilized by phosphate. *Nancy Gough*

1384. **The Role of Epinephrine in the Secretion of the Adrenal Cortex**
H. GERSHBERG, E. G. FRY, J. R. BROBECK, and C. N. H. LONG. *Yale Journal of Biology and Medicine* [*Yale J. Biol. Med.*] **23**, 32–51, Sept., 1950. 37 refs.

For some years it has been known that release of adrenocorticotrophin (ACTH) is associated with increased activity of the autonomic nervous system and concomitant release of adrenaline, and this may be the mechanism whereby adequate amounts of adrenal cortical hormone are rapidly made available to the body. The present authors have attempted to determine (*a*) whether adrenaline acts directly on the adrenal cortex or through the anterior pituitary in increasing adrenal cortical secretion; and (*b*) if, as seems likely, the latter is the case, whether adrenaline provokes the secretion of ACTH directly, or indirectly by enhancement of the utilization of cortical hormone by the tissues.

The secretory activity of the adrenal cortex of albino rats was estimated by measuring the adrenal cholesterol and ascorbic-acid content, both of which fall when the blood level of ACTH is increased. Intraperitoneal or intramuscular infusion of as little as 0·08 μg. of adrenaline per kg. body weight per hour caused a marked fall in adrenal cholesterol and ascorbic-acid levels in normal, but not in hypophysectomized, rats. A similar decrease was produced by the release of endogenous adrenaline by subjection of the animals to haemorrhage, cold, painful stimulation, or insulin hypoglycaemia. Again this effect was dependent on the presence of the anterior lobe of the pituitary and could not, therefore, be due to direct action on the adrenal cortex.

Pretreatment of the animals with cortical extracts (but not with deoxycortone acetate) prevented adrenal activation during adrenaline secretion. Experiments showed that this blocking action of cortical extract did not operate through a metabolic process such as gluconeogenesis, but by direct action on the pituitary. Rats from which the adrenal medulla had been removed were used in studying the secretion of ACTH in the absence of adrenaline. It was found that the cortex could still be stimulated, but that the response was greatly delayed. *Nancy Gough*

1385. **The Secretion of the Adrenal Medulla at Rest and during Carotid Occlusion.** (Über die Sekretion des Nebennierenmarkes in Ruhe und beim Abklemmen beider Carotiden)
F. BRAUNER, F. BRUCKE, F. KAINDL, and A. NEUMAYR. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **83**, 505–519, Sept., 1950. 3 figs., 15 refs.

Writing from the Pharmacological Institute of Vienna, the authors describe a new test for adrenaline and noradrenaline. The tail of the anaesthetized cat is lightly fixed, and the movements of hairs at the base of the tail are recorded following injection of drugs such as adrenaline into the tail artery. The shadows cast by the hairs are used to measure the response of the arrector pilae muscles in terms of the angle between the resting and stimulated positions of the hairs. In such a preparation DL-adrenaline is 6 to 8 times as potent as DL-noradrenaline. Blood from the adrenal veins was tested before and during occlusion of both carotid arteries. Its adrenaline equivalent was determined on the tail-hair preparation and also on rabbit intestine.

During bilateral carotid occlusion the amount of adrenaline equivalent in the adrenal venous blood rose from 0·082 to 0·213 μg. per kg. per minute, tested on the tail-hair. With the rabbit-intestine test lower values were obtained, particularly during carotid occlusion. Since the relative activities of noradrenaline and adrenaline on tail-hair and rabbit intestine are respectively 1 to 6 and 1 to 2, these results do not support the findings of Holtz who considered that the substance secreted by the adrenal during carotid occlusion was mainly noradrenaline. If this were so, in the present experiments higher figures would have been obtained with the rabbit-intestine technique than with the cat tail-hair method, especially during carotid occlusion. *Derek R. Wood*

1386. **Adrenal Medullary Hormones in Water Diuresis**
A. D. HORRES, W. J. EVERSOLE, and M. ROCK. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 58–61, Oct., 1950. 15 refs.

The effect of adrenaline and noradrenaline on the water diuresis of rats given 3 ml. of water per 100 g. weight is described. The experiments were carried out at Syracuse University. The adrenal hormones, suspended in peanut oil, were injected subcutaneously in doses of 3 or 30 μg. per 100 g. weight. Control rats received injections of peanut oil only.

Noradrenaline caused the greatest increase in diuresis. Commercial adrenaline (consisting mainly of L-adrenaline but containing traces of noradrenaline) also increased diuresis, but to a lesser extent. Pure L-adrenaline had no stimulating action. In intact rats "dibenamine" caused water retention, blocking the diuretic effect of commercial adrenaline. The diuresis caused by noradrenaline was, however, only partially blocked by dibenamine. Removal of the adrenal medullae did not prevent the diuretic response due to noradrenaline, but dibenamine no longer blocked diuresis in these rats.
G. Ansell

PITUITARY

1387. **Two Types of Basophils in the Anterior Pituitary of the Rat and their Respective Cytophysiological Significance**
N. S. HALMI. *Endocrinology* [*Endocrinology*] **47**, 289–299, Oct., 1950. 8 figs., 26 refs.

The 2 types of basophil cells (beta and delta cells) distinguished by Lomas in the pituitary of the rat have been further studied by the author by means of a new staining technique (aldehyde-fuchsin combined with a modified azan method). When light green is substituted for aniline blue in the azan technique, the result of this staining method is as follows: nuclei red, acidophil granules orange, beta-cell granules violet, delta-cell granules green, and cytoplasm of chromophobes unstained or pale grey-green. An attempt was made to correlate morphology and function in the pituitary by subjecting rats (Sprague–Dawley strain) to various procedures known to modify the secretion of anterior-lobe hormones, and subsequently examining the pituitary microscopically. The delta-cell count of the female pituitary was considerably lower than that of the male. Castration or thyroidectomy of male rats led to a marked increase in number, progressive hyperplasia, and vacuolation of the delta cells. These observations suggest that the delta cells elaborate follicle-stimulating hormone and possibly thyrotrophin. The beta cells were equally numerous in both sexes, remained unaffected by castration, and tended to decrease in number after thyroidectomy.

Experiments designed to determine the site of elaboration of adrenocorticotrophin (ACTH) were inconclusive. Hemiadrenalectomy and subsequent exposure to cold led to some increase and enlargement of the beta cells suggesting hyperfunction, but prolonged treatment with deoxycortone acetate, said to depress the output of ACTH, increased both the delta-cell and the beta-cell counts. Total adrenalectomy caused an increase in the number of acidophil and delta cells and a slight decrease in that of the beta cells. The author concludes that although the site of formation of ACTH may be in the beta cells, the problem requires further investigation.

Nancy Gough

1388 (*a*). **Pituitary Gland and Blood Lymphocytes**
H. F. COLFER, J. DE GROOT, and G. W. HARRIS. *Journal of Physiology* [*J. Physiol., Lond.*] **111**, 328–334, Oct. 16, 1950. 1 fig., 20 refs.

To establish the usefulness of the lymphopenic response as an index of adrenocorticotrophin (ACTH) secretion by the anterior pituitary gland, preliminary experiments were carried out at the University of Cambridge to investigate the effects of emotional stress on rabbits. Subcutaneous faradic stimulation over the lumbar vertebrae, or placing the unanaesthetized animal in restraining clamps for 1 to 2 hours, served as the stress stimulus. In normal rabbits such stress always led to lymphopenia, the absolute lymphocyte count falling to about 70% of its initial value in 3 hours. There was usually an accompanying granulocytosis, but the erythrocyte count did not change. Hypophysectomy led to an abolition of the lymphopenic response to stress in all animals when tested within 2 weeks of operation During this time, however, the injection of ACTH caused the usual reduction in the lymphocyte count. Of 8 animals tested more than 2 weeks after operation 4 still showed no response. In these, the hypophysectomy had been complete. In the remaining 4 animals, in which some response was obtained, post-mortem examination showed the hypophysectomy to have been incomplete.

The intravenous injection of 1 ml. of 1-in-150,000 adrenaline into 7 normal rabbits gave rise to a lymphopenic response in one case. Denervation of the adrenal glands did not impair the lymphopenic response. It is concluded that a reduction in the lymphocyte count can be used as an index of anterior pituitary secretion in experimental work, provided that the subject is not exposed to incidental emotional stress. *P. Mestitz*

1388 (*b*). **Hypothalamic Control of the Anterior Pituitary Gland and Blood Lymphocytes**
J. DE GROOT and G. W. HARRIS. *Journal of Physiology* [*J. Physiol., Lond.*] **111**, 335–346, Oct. 16, 1950. 13 figs., 20 refs.

A technique is described which permits the electrical stimulation of various parts of the hypothalamus and anterior pituitary gland by remote control in the conscious, quiescent, experimental animal without subjecting it to any emotional stress. In essence, this involves keeping the unrestrained animal in a wooden cage which is actually in the field of a large primary coil, the small secondary being implanted in the animal's skull.

[The original paper should be consulted for the details of the method.] A large number of experiments were performed on rabbits, in each of which stimulation was carried out for one hour and the effects on the blood count observed, at least three experiments being carried out on each animal (see Abstract 1388 (*a*)).

Stimulation of the posterior part of the tuber cinereum or mamillary body produced a lymphopenic response, similar to that following emotional stress, which was not impaired by bilateral cervical sympathectomy. There was no such response to stimulation of the supraotico-hypophysial tract, infundibular stem, pars distalis and pars intermedia, zona tuberalis and pars tuberalis, or the lateral and anterior regions of the tuber cinereum. Lesions of the zona tuberalis completely abolished the lymphopenic response to emotional stress. Complete destruction of the infundibular stem and subtotal destruction of the pars distalis and pars intermedia were compatible with a normal response. Lesions extending transversely in the posterior region of the tuber cinereum or in the mamillary body often caused loss or diminution of the response. It is concluded that the secretion of the anterior pituitary hormone involved in the lymphopenic response (probably adrenocorticotrophin) is under neural control through the hypothalamus and the hypophysial portal vessels of the pituitary stalk.

P. Mestitz

Pharmacology and Therapeutics

1389. **Evaluation of Curarizing Drugs in Man. IV. Tri-(diethylaminoethoxy)-1 : 2 : 3 Benzene (Flaxedil)**
K. R. UNNA, E. W. PELIKAN, D. W. MACFARLANE, and M. S. SADOVE. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 201–209, Oct., 1950. 15 refs.

Tri-(diethylaminoethoxy)-1 : 2 : 3 : benzene (" flaxedil ") was administered intravenously to volunteers and the effects on grip strength, respiration, pulse, and blood pressure were compared with those previously recorded for D-tubocurarine (DTC) and decamethylene-bis-(trimethylammonium) bromide (" C10 "). On grip strength it had 25 to 27% of the effect of DTC, but the duration of action was shorter. Effects on respiration were the same for both. It caused an increase in heart rate and blood pressure. A second dose, given after complete recovery, had a much more potent action than the first dose. All its effects were antagonized by physostigmine, contrasting in this respect with C10. One subject who was especially sensitive to flaxedil and DTC had no special sensitivity to C10. *V. J. Woolley*

1390. **Evaluation of Curarizing Agents in Man**
K. R. UNNA, E. W. PELIKAN, D. W. MACFARLANE, R. J. CAZORT, M. S. SADOVE, and J. T. NELSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 448–451, Oct. 7, 1950. 6 figs., 7 refs.

Owing to the great variation in the effects produced by curarizing drugs in different species, some 150 experiments were performed on young, healthy, unanaesthetized, male subjects. The drugs employed were D-tubocurarine chloride (DTC), dimethyltubocurarine iodide (dimDTC), decamethonium bromide (" C10 "), and gallamine (" flaxedil "), all given by slow intravenous injection. The points under examination included determination of the dose needed to reduce the strength of the handgrip by 95%, and the effects of this dose upon the rate and minute volume of respiration, the mean tidal volume, and the vital capacity.

Judged by its effects on the grip strength, decamethonium bromide proved to be 2, 5, and more than 20 times as strong as dimethyltubocurarine, D-tubocurarine, and flaxedil respectively, though its effects were less constant and predictable than were those of the other drugs. Again, when gauged by its power of reducing vital capacity, decamethonium depressed the respiration much more than the others, so that adequate paralysis of striated muscle, as judged by the handgrip strength, was only attained with a decrease of the vital capacity to less than one-half of the normal, while a similar dose of flaxedil or of dimethyltubocurarine caused a reduction of only one-fifth or less. This effect of decamethonium is exactly the opposite of the " respiration-sparing " action claimed for it in cats and monkeys. The duration of its action on striated muscle, judged by the time required for the handgrip strength to return from 5% to 75% of the normal, was least with decamethonium (20 minutes) and most with D-tubocurarine (27 minutes).

Cumulative effects were observed with the drugs D-tubocurarine and dimethyltubocurarine in that a weakening of the handgrip strength about equal to that recorded before was produced by about one-half of the original dose given 45 minutes after all measurable effects of the first dose had disappeared. On the other hand, decamethonium, when given in a similar manner, produced a significantly smaller effect. Tachyphylaxis to this drug, therefore, not previously seen in animals, occurs in man. Neostigmine in a dose of 0·75 mg. was found to reduce, but not to abolish, the effects of D-tubocurarine, as a dose of the latter which would normally reduce the power of the handgrip 95% would only reduce it by about 35% after neostigmine had been given. Decamethonium is not antagonized by neostigmine, but when given after recovery from the effects of D-tubocurarine it is without any curarizing power. In animals it is claimed that pentamethonium iodide antagonizes the effects of decamethonium, but this was not found to occur in man, the previous administration of 50 mg. of the former causing no diminution in the effects of the latter. *Reginald St. A. Heathcote*

1391. **Studies on the Inter-relationship of Certain Cholinergic Compounds. IV. Anti-curare Action in Anesthetized Man**
J. F. ARTUSIO, W. F. RIKER, and W. C. WESCOE. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 227–237, Oct., 1950. 6 figs., 9 refs.

1392. **The Fate of Intrathecal Procaine and the Spinal Fluid Level Required for Surgical Anesthesia**
M. HELRICH, E. M. PAPPER, B. B. BRODIE, M. FINK, and E. A. ROVENSTINE. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 78–82, Sept., 1950. 3 figs., 5 refs.

Procaine hydrochloride (150 mg.) was injected into the spinal theca through the 4th interspace in normal subjects and samples of cerebrospinal fluid were withdrawn from various higher levels by means of a ureteric catheter introduced through the 3rd space. It was found that the concentration of procaine decreased uniformly with distance from the site of injection, and it was confirmed that no breakdown products of procaine were present in the fluid. The chief breakdown product, *p*-aminobenzoic acid, was found in gradually increasing quantity in the blood and urine. Concentration of procaine at various levels was correlated with cutaneous sensibility, and it was found that a concentration of 0·2 mg. per ml. was necessary for analgesia.
V. J. Woolley

1393. **The Effect of Cyclopropane, Ether, and Thiopental Sodium upon the Over-digitalized Heart**
L. MOSEY and J. W. STUTZMAN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 34–37, Oct., 1950. 8 refs.

The authors, working at the Boston University School of Medicine, have compared the effects of cyclopropane, ether, and thiopentone sodium upon cardiac arrhythmia due to over-digitalization in dogs. Of 12 dogs (5 to 13 kg.), 4 were digitalized with 0·3 mg. of digitoxin per kg. body weight and 8 with 0·07 to 0·08 mg. of G-strophanthin per kg. intravenously. The dogs were anaesthetized with 28 to 31% cyclopropane in oxygen by rebreathing, with ether on a gauze mask, or with thiopentone sodium (25 to 30 mg. per kg.) intravenously. The cyclopropane improved or abolished the arrhythmia, ether caused a reversion to normal rhythm, while thiopentone exerted no effect upon the electrocardiographic abnormalities. *Malcolm Woodbine*

1394. **A Comparison of the Anticonvulsant Actions of Some Phenylhydantoins and their Corresponding Phenylacetylureas**
E. A. SWINYARD and J. E. P. TOMAN. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 151–157, Oct., 1950. 16 refs.

Nine phenylhydantoins and related phenylacetylureas were examined as to: (1) solubility; (2) the minimum dose causing incoordination in rats; (3) effect on electric and " metrazol " convulsions in rats; and (4) ability to suppress hyperexcitability caused by phosphate in frog sciatic nerve. Diphenylacetylurea is very insoluble and had very little action in any of these respects. The other eight compounds all showed some potency in all the tests, but no correlation could be found between the results of the various tests and solubility or structure. It is not necessary to postulate a closure or opening of the ring structure in these compounds, since phenyldimethylacetylurea is as effective as the others and is incapable of closure, while the open compounds are no more effective than the hydantoins. *V. J. Woolley*

1395. **Pain Relief with Hypnotic Doses of Barbiturates and a Hypothesis**
A. S. KEATS and H. K. BEECHER. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 1–13, Sept., 1950. 23 refs.

A comparison of the pain-relieving properties of intravenously injected pentobarbitone, morphine, and saline was made in patients with severe and persistent post-operative pain. The effect of each drug was assessed 30 minutes after being given, and if little or no relief was obtained the next drug in the series was injected. If relief was obtained, then the next drug was injected as soon as the pain had returned to its initial level. If the pain did not return, or was qualitatively different from the initial pain on its return, the subject was regarded as unsuitable for further testing. Pentobarbitone was given in doses of 60 and 90 mg. per 70 kg. body weight, and morphine in doses of 8 mg. per 70 kg. Five groups were studied, each made up of 30 to 34 subjects, and differing from each other in the dose of pentobarbitone given and order of administration of the three drugs.

Pentobarbitone relieved post-operative pain in approximately 50% of cases, saline in 20%, and morphine in 80%. A distinction is made between " pain " and " suffering ", and it is suggested that pentobarbitone acts as an analgesic by depressing the internuncial spread of pain impulses in the brain and by inhibiting the psychic phase of pain experience. *P. A. Nasmyth*

1396. **An Estimation of the Activity of Analgetic Materials**
D. D. BONNYCASTLE and C. S. LEONARD. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 141–145, Oct., 1950. 2 figs., 6 refs.

1397. **Effects of Oral Hexamethonium Salts on Gastric Secretion**
A. W. KAY and A. N. SMITH. *British Medical Journal* [*Brit. med. J.*] **2**, 807–809, Oct. 7, 1950. 5 figs., 2 refs.

The inhibiting effect of the intramuscular injection of hexamethonium iodide on gastric acidity and motility has been previously described by the authors (*Brit. med. J.*, 1950, **1**, 460). The effect of oral administration of the drug is now reported.

Ten patients with duodenal ulceration were given a single dose of 500 mg. of hexamethonium iodide by stomach tube after removal of the fasting juice. Specimens withdrawn one hour (or, in 4 cases, 2 hours) later, showed no fall in acidity in 2 cases, while 5 patients had achlorhydria lasting up to 4 hours and in 3 there was reduced acid secretion as compared with preliminary control tests. To another group of 4 patients the same dose was given on 2 successive days, a similar fall in acidity being observed on each occasion. The effects of 440 mg. of the bromide and of 340 mg. of the chloride were compared with that of 500 mg. of the iodide in 6 cases, the iodide causing the greatest fall. The side-effects observed after administration of hexamethonium iodide by mouth on 36 occasions were less than after intramuscular injection, but included blurred vision, due to paralysis of accommodation, and mild postural hypotension developing after one hour and rarely giving rise to symptoms.

[The scale of this investigation appears small.]
K. Gurling

1398. **Multiple-balloon-kymograph Recording of Variations in Motility of the Upper Small Intestine in Man during Long Observation Periods before and after Placebo Administration**
W. P. CHAPMAN, E. N. ROWLANDS, A. TAYLOR, and C. M. JONES. *Gastroenterology* [*Gastroenterology*] **15**, 341–355, June, 1950. 6 figs., 13 refs.

At Harvard Medical School, Boston, Massachusetts, observations were made, in 12 normal adults, of the motility of the upper part of the small intestine by means of the multiple-balloon water-manometer technique. After a control period, a tablet or a subcutaneous injection of an inert substance was administered without verbal suggestion. Propulsive and total contractions decreased by an average of 32% and 24% respectively

with the passage of time. In general, variations in tonus were smaller than those in contractile activity; " spasms " (sudden increases in tonus) were associated with more or less prolonged periods of diminution of contractions. The character of the motility pattern was often fairly constant for a given individual. The purpose of this study was to provide a basic control for projected studies of the effects of drugs on the motility of the human small intestine, in which a similar technique will be used. *R. A. Gregory*

1399. **Anticonvulsant Properties of Benadryl and Pyribenzamine**
E. A. SWINYARD, J. M. JOLLEY, and L. S. GOODMAN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 239–242, Oct., 1950. 20 refs.

The authors, working at the University of Utah Colleges of Pharmacy and Medicine, examined the anticoagulant properties of diphenhydramine (" benadryl ") and tripelennamine (" pyribenzamine ") on male albino rats, giving the drugs orally (in suspension in 10% gum acacia) and intraperitoneally and comparing their effect with that of phenytoin (" dilantin "). The anticonvulsant potency of each drug (at previously determined times of peak effect) was measured by determining its ability to abolish the tonic extensor component of maximal electrically-induced seizures and to protect the animals from the convulsant effect of the subcutaneous administration of 70 mg. per kg. of leptazol (" metrazol "). In addition, the minimal neurological toxicity (loss of placing responses, ataxia, depression) was determined and a " protective index " (P.I.) calculated as the ratio of minimal neurological toxicity to anticonvulsant potency. In descending order of P.I., phenytoin, tripelennamine, and diphenhydramine were all found to modify the maximal electric-shock seizure pattern, but not to prevent leptazol convulsions.
Malcolm Woodbine

1400 (*a*). **The Comparative Effects of Small Intravenous Doses of Epinephrine upon Arterial Pressure and Pulse Rate in Normotensive Subjects and in Hypertensive Patients before and after Thoracolumbar Sympathectomy**
W. E. JUDSON, J. W. CULBERTSON, C. M. TINSLEY, J. LITTER, and R. W. WILKINS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1405–1413, Oct., 1950. 8 figs., 17 refs.

The effects of adrenaline on the cardiovascular system before, and early after, sympathetic denervation of the splanchnic bed have been studied in hypertensive patients by means of continuous records of intra-arterial blood pressure, pulse rate, and respiration. The first two of these were made by means of a needle inserted into the brachial artery, and a continuous-drip infusion of saline solution was given into an anterior cubital vein whereby single doses of adrenaline (0·5 to 50 μg.) were injected intravenously when the readings had become stationary. The responses of 5 normotensive subjects and of 13 hypertensive patients, of whom 6 were studied again at least 10 days after the second stage of a lumbodorsal sympathectomy, showed no qualitative differences as between the two groups or, in the latter group, between pre- and post-operative observations. Small intravenous doses of adrenaline produced a three-phase response: (1) a hypertensive first phase occurring usually 15 to 25 seconds after injection; (2) a transient, hypotensive, second phase usually present at 25 to 35 seconds; (3) a more sustained, hypertensive, third phase observed at 55 to 70 seconds after injection. There were slight differences in the pulse-rate responses in the various groups, but it was clear that the hypertensive patients were not more sensitive to adrenaline than the normotensive subjects and did not become more sensitive after thoracolumbar sympathectomy. *G. B. West*

1400 (*b*). **The Comparative Effects of Small Intravenous Doses of L-Norepinephrine upon Arterial Pressure and Pulse Rate in Normotensive Subjects and in Hypertensive Patients before and after Thoracolumbar Sympathectomy**
W. E. JUDSON, F. H. EPSTEIN, and R. W. WILKINS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1414–1420, Oct., 1950. 4 figs., 19 refs.

The cardiovascular effects of noradrenaline in normal subjects and before and after sympathetic denervation of the splanchnic bed in hypertensive patients have been studied (see Abstract 1400 (*a*)). A single intravenous dose produced a single-phase hypertensive response with a proportionate rise in both systolic and diastolic blood pressure, the responses being similar in the 5 normotensive subjects and in the 6 patients with essential hypertension both before and after sympathectomy. The resting mean arterial pressure was, in general, moderately lowered in the hypertensive patients after splanchnicectomy. In the normotensive subjects the pulse rate decreased after an intravenous dose of noradrenaline (0·25 to 15 μg.), but in the hypertensive patients before operation the rate was either maintained or decreased only slightly. After splanchnicectomy the same patients conformed more to the normotensive pattern, the pulse being significantly slowed by noradrenaline.

[These results are in disagreement with those of other workers, who have found that in hypertensive patients the response of the systolic and mean arterial pressures to the administration of noradrenaline is always greater than in normotensive subjects. However, the number of subjects in each group in the present study was very small.] *G. B. West*

1401. **Potentiation of Pressor Effects of Norepinephrine and Epinephrine in Man by Desoxycorticosterone Acetate**
W. RAAB, R. J. HUMPHREYS, and E. LEPESCHKIN. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1397–1404, Oct., 1950. 2 figs., 33 refs.

It is known that sub-threshold doses of adrenaline have a pressor effect on the intact dog and cat after pretreatment with adrenal cortical extract. In man the pressor effect of subcutaneous injections of adrenaline is markedly intensified after several daily doses of 10 to 50 mg. of deoxycortone acetate (DCA) have been given. The effect of intravenous infusions of adrenaline and

noradrenaline before and after the injection of 10 mg. of DCA intramuscularly for 17 days has now been studied in 15 physically normal male subjects, whose resting blood pressure had remained practically unchanged by the DCA treatment. The adrenaline and noradrenaline were given at a dosage of 0·1, 0·2, and 0·3 μg. per kg. body weight per minute for 5-minute periods.

With adrenaline the average elevation of systolic blood pressure brought about at these dosage levels was 6, 17, and 27 mm. Hg respectively; the diastolic pressure was depressed by 8 mm. Hg by the small dose, remained unchanged with the intermediate dose, and was increased by 8 mm. Hg by the high dose. After treatment with DCA the average depression of diastolic pressure by the small dose of adrenaline was transformed into a slight elevation, and all systolic and diastolic pressor responses were increased significantly. With similar doses of noradrenaline before treatment the systolic pressure was raised to a degree similar to that observed with adrenaline, but the diastolic pressure was raised without exception and to a much greater degree. After treatment with DCA the systolic pressor effect of noradrenaline was intensified to about the same degree as that of adrenaline, and the diastolic effect was also increased. These findings may be of value in the elucidation of the factors concerned in the production of essential hypertension. *G. B. West*

1402. **Pharmacological and Toxicological Studies on 2-(N-*p*′-Tolyl-N-(*m*′-hydroxyphenyl)-aminomethyl)-imidazoline (C-7337), a New Adrenergic Blocking Agent**
J. H. TRAPOLD, M. R. WARREN, and R. A. WOODBURY. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 119–127, Oct., 1950. 16 refs.

This substance, in doses of 0·8 to 1 mg., reverses the pressor response to 50 mg. of adrenaline in dogs. The pressor response is restored by 5 to 10 mg. of ephedrine, amphetamine, " vonedrine," or " tuamine," but not by further adrenaline. It abolishes the response of the nictitating membrane to stimulation of the cervical sympathetic and the hyperglycaemic response to adrenaline. It is only slightly toxic, symptoms being mainly due to hypoglycaemia. The LD 50, causing death in one week, is about 100 mg. twice daily. Adrenergic block comes on more quickly and is less lasting than that due to " dibenamine ". It has no effect on the blood-pressure changes caused by histamine or acetylcholine. *V. J. Woolley*

1403. **A Comparison of the Sympathetic Inhibitory Action of 1-(3 : 4-Dihydroxyphenyl)-2-aminoethanol [" Isoprenaline "] with that of Several of its Analogs.** [In English]
A. M. LANDS, F. P. LUDUENA, E. ANANENKO, and J. I. GRANT. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **83**, 602–616, Sept., 1950. 7 figs., 25 refs.

Sympathetic inhibitory activity was studied by finding the doses of substances effective in preventing bronchoconstriction due to histamine in perfused guinea-pig lungs, contraction of the rat uterus due to posterior pituitary extract, and relaxation of isolated guinea-pig intestine. Vasodepressor activities were compared in anaesthetized dogs. The compounds are classed as (1) strongly inhibitory—*iso*propylnoradrenaline (" isoprenaline "), adrenaline, and noradrenaline; and (2) weakly inhibitory—3 : 4-dihydroxyphenylmethylamine (" épinine "), methylaminoacetopyrocatechine (" kephrine ") and *iso*propylhydroxytyramine. The activity of the weaker compounds is comparable to that of papaverine. Inhibitory activity is increased by the presence of a hydroxyl group on the side-chain and by N-alkyl substitution. In most organs adrenaline has higher excitatory and inhibitory sympathetic activity than noradrenaline and may be considered to represent a biological compromise. It is suggested that the predominant effect of adrenaline at any site is determined by its concentration and the " receptor pattern of the end organ ". *Derek R. Wood*

1404. **Observations on Automatic Participation in Pulmonary Arteriolar Resistance in Man**
N. O. FOWLER, R. N. WESTCOTT, V. D. HAUENSTEIN, R. C. SCOTT, and J. MCGUIRE. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1387–1396, Oct., 1950. 2 figs., 13 refs.

It is known that the tetraethylammonium ion blocks transmission in autonomic ganglia, both sympathetic and parasympathetic. The depressor effect of tetraethylammonium on systemic systolic and diastolic blood pressure appears to result from the inhibition of vasoconstrictor tone, which is much more pronounced in the systemic circulation when hypertension is present. In view of these effects on the systemic circulation, the effect of tetraethylammonium chloride upon the pulmonary arteriolar resistance was investigated in a series of 15 subjects, 5 being normal and the remaining 10 being patients with cardiovascular or pulmonary disease. Cardiac catheterization was performed by the method of Cournand and Ranges (*Proc. Soc. exp. Biol., N.Y.*, 1941, **46**, 462), a double-lumen catheter being used in order that pulmonary capillary pressure and pulmonary arterial pressure could be measured simultaneously. Pulmonary capillary pressure was determined by the method of Hellems *et al.* (*Amer. J. Physiol.*, 1948, **155**, 98). The catheter was advanced into a branch of the pulmonary artery as far as possible, so that the branch was occluded and the pressure distal to the point of occlusion was measured. Simultaneous electrocardiograms, ballistocardiograms, and records of the brachial arterial, pulmonary arterial, and pulmonary capillary pressure were made by means of a five-channel optical oscillograph. Cardiac output was determined by the direct Fick method. Samples of expired air and of blood from the brachial and pulmonary arteries were taken for estimation of carbon dioxide and oxygen content.

After control records and samples had been taken, the subjects were given 5 or 6 mg. of tetraethylammonium chloride (TEA) per kg. intravenously. When the maximum effect upon the blood pressures had been obtained (3 to 5 minutes later), blood and gas samples were again collected for cardiac-output estimation. Of

15 patients studied, the mean pulmonary artery pressure was lowered by TEA in 11, in all but one of whom pulmonary hypertension had previously been present. In the other 4 patients the mean pulmonary arterial pressure was initially normal (13 to 17 mm. Hg) and no decline was observed after the administration of TEA. In 4 out of 6 patients with pulmonary hypertension, TEA caused a significant decrease in pulmonary arteriolar resistance. The effect of TEA upon the cardiac output was variable, but a decline in mean brachial arterial pressure was seen in each of the 14 patients. The failure of pulmonary arteriolar resistance to decline following the intravenous injection of TEA in 4 out of the 5 normal subjects suggests that the autonomic nervous system may not be an important factor in the maintenance of normal pulmonary arteriolar resistance. Further observations on normal subjects are needed to substantiate this suggestion.

G. B. West

1405. **Binding of the Mercury of an Organic Mercurial Diuretic by Plasma Proteins**

J. P. MILNOR. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 63–65, Oct., 1950. 11 refs.

Using a mercurial diuretic (" mercuhydrin ") prepared with radioactive mercury, the author has examined the diffusion of the mercury across a semi-permeable membrane *in vitro*. Solutions of the diuretic in Ringer's solution, reconstituted human plasma (7·3 g. per 100 ml. total protein), fresh human plasma, and human urine were used. The extent of the binding of the mercury by plasma proteins was proportional to the concentration of the mercurial. At dilutions of 1 in 1,000 or more over 90% of the mercury was bound; at 1 in 100 or less 50% of the mercury was free.

Malcolm Woodbine

1406. **Evaluation of Some Drugs in Motion Sickness**

H. I. CHINN, B. A. STRICKLAND, F. W. OBERST, S. S. WILKS, and M. TINKHAM. *Journal of Aviation Medicine* (*J. Aviat. Med.*] **21**, 424–429, Oct., 1950. 2 figs., 10 refs.

CHEMOTHERAPY

1407. **Aureomycin in Prevention of Bacteremia following Tooth Extraction**

O. ROTH, A. L. CAVALLARO, R. H. PARROTT, and R. CELENTANO. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 498–504, Oct., 1950. 14 refs.

The commonest organism causing subacute bacterial endocarditis is *Streptococcus viridans*, which is normally present in the mouth and particularly in the presence of gum infection and dental caries. Extraction of a tooth may thus result in a temporary bacteraemia, giving the organism the opportunity to implant itself on damaged or abnormal endocardium. Sulphonamides and penicillin have been used to prevent such bacteraemia in patients with heart lesions requiring dental treatment, but not always with success, and the search has continued for a preparation that is non-toxic, will not cause organisms to become resistant, and can be given by mouth. Aureomycin appears to meet these requirements.

For the purposes of this study 50 dental patients without any cardiac disease and needing an extraction were carefully examined and classified into four groups with varying degrees of dental infection. Alternate patients were given aureomycin from the day before operation until the day after, 0·5 g. being given 6-hourly, the average total dose being 3·0 g., and the usual interval between the last pre-operative dose and the extraction being 3 hours. General anaesthesia was induced with thiopentone and oxygen, supplemented with nitrous oxide. The blood was examined bacteriologically before and after operation. Of the 25 untreated cases, in 14 the blood culture was positive for *Strep. viridans* immediately following extraction, whereas of the 25 treated cases in only one case was the blood culture positive for *Strep. viridans*. The authors therefore advise the prophylactic administration of aureomycin to all patients with cardiac disease on whom dental operations are necessary.

[The authors suggest that, contrary to general usage in Great Britain, local analgesia with procaine and adrenaline should be used for patients suffering from heart disease rather than general anaesthesia.]

D. Robertson-Ritchie

1408. **Effect of Aureomycin on the Clotting Time of the Blood**

J. B. SHAPSE and L. T. WRIGHT. *Angiology* [*Angiology*] **1**, 306–311, Aug., 1950. 1 fig., 7 refs.

There is conflicting evidence as to the effect of aureomycin on the clotting time of the blood. Thirty patients were therefore given 500 mg. of aureomycin twice daily. Clotting times were determined by the Lee and White method at intervals of approximately 6, 12, 24, and 48 hours after the initial dose. Clotting times in the majority of patients showed a slight increase during the first 12 hours, returned approximately to normal at 24 hours, and again increased at 48 hours. The average increase in clotting times at 12 and 24 hours was 1½ minutes and the maximum increase was 3½ minutes. These changes are not of clinical significance.

A. W. H. Foxell

See also Section Infectious Diseases, Abstracts 1708, 1739.

1409. **Marcescin, an Antibiotic Substance from *Serratia marcescens***

A. T. FULLER and J. M. HORTON. *Journal of General Microbiology* [*J. gen. Microbiol.*] **4**, 417–433, Sept., 1950. 14 refs.

Marcescin is a colourless thermostable polypeptide which can be extracted from culture media in which *Serratia marcescens* (*Bacillus prodigiosus*) has been grown. If the organism is grown in broth the substance can be fairly readily extracted after preliminary adsorption on to charcoal, but the yield is not very great. The most suitable medium for high yields is an ammonium citrate–glycerol medium, but the extraction and purifica-

tion of the antibiotic obtained by this means is a more complicated procedure. This antibiotic is not to be confused with the antibacterial substance previously associated with *B. prodigiosus*, which was the red pigment prodigiosin.

Marcescin is an active inhibitor of growth of a number of bacteria. The inhibiting activity ranges from $<0{\cdot}01$ μg. per ml. in the case of *Corynebacterium diphtheriae* to $3{\cdot}2$ μg. per ml. in the case of *Bacterium coli*. Marcescin seems to have the effect of diminishing the size of the cells in bacterial growths, and to make some Gram-positive bacteria become Gram-negative and also rough. One of the characteristic properties would appear to be the ease with which most bacteria absorb marcescin. Because of this property it has not yet been possible to show whether the antibacterial activity is bactericidal or bacteriostatic.

The antibiotic is toxic to laboratory animals, particularly mice. The LD 50 for mice was 125 mg. per kg. by subcutaneous injection, and sublethal doses failed to protect mice against various marcescin-sensitive strains of bacteria. *H. J. Bensted*

See also Section Hygiene and Public Health, Abstract 1349; and Section Digestive Disorders, Abstract 1609.

TOXICOLOGY

1410. **Lead Poisoning in Infancy**
N. S. CLARK. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **25**, 297–301, Sept., 1950. 3 figs., 12 refs.

A 4-month-old infant developed lead encephalopathy from drinking water contaminated with lead from the pipes of a domestic supply. Symptoms followed shortly after the change from breast to bottle feeding. Complete recovery ensued in hospital, and a 3-year follow-up has revealed no residua. *M. MacGregor*

1411. **Seven Cases of Barium Carbonate Poisoning**
G. DEAN. *British Medical Journal* [*Brit. med. J.*] **2**, 817–818, Oct. 7, 1950. 15 refs.

A wholesale druggist put barium carbonate, a rat poison, into a barium sulphate container in error, and 7 cases of poisoning followed its use for making up barium meals. One patient died, his condition probably being made worse by administration of curare and anaesthetics for the removal of a bone in the oesophagus. This patient swallowed only about 1·7 oz. (53 g.) of barium carbonate, but the 6 others took 4·26 oz. (133 g.) which is above the known lethal dose. The symptoms included vomiting, diarrhoea with colic, a peculiar stiffness of the face with blurred vision, a desire to micturate, and intense weakness of the limbs. Although the patients were apparently shocked, the diastolic blood pressure in 3 cases was above 100 mm. Hg. The pulse was thready but slow, and often irregular. In one case an electrocardiogram showed multiple extrasystoles. The mental state was normal; none suffered from fits, and apart from weakness of the limbs lasting up to one week there were no abnormal signs in the nervous system. Three patients who took magnesium sulphate experienced less severe symptoms, and this seems a good antidote. The toxic effects appeared to be mainly on smooth and striated muscles, with no true neurological involvement. Barium carbonate might well be distinctively coloured.
K. Gurling

1412. **Use of Intravenous Amphetamine Sulphate in Acute Barbiturate Poisoning**
J. D. N. NABARRO. *British Medical Journal* [*Brit. med. J.*] **2**, 924–926, Oct. 21, 1950. 17 refs.

Details are given of 3 cases of barbiturate poisoning treated with picrotoxin and intravenous amphetamine sulphate. An asthmatic in coma following the ingestion of 12½ gr. (0·8 g.) of barbiturate responded to amphetamine alone. A woman in deep coma due to taking 80 gr. (5·3 g.) of amylobarbitone became conscious when 70 mg. of amphetamine was given, although treatment with 200 mg. of picrotoxin in 17 hours had failed. Another deeply comatose patient who had taken 96 gr. (6·3 g.) of phenobarbitone was given both drugs together. Muscular twitching was induced, but consciousness was not restored until a total of 1·08 g. of picrotoxin and 4·23 g. of amphetamine had been given over a period of 121 hours.

Intravenous amphetamine in doses of 20 mg. is considered a useful adjunct to picrotoxin in the treatment of barbiturate poisoning, particularly when the latter has produced facial twitching. Suggestions for the general management of barbiturate poisoning are given.
K. Gurling

1413. **An Adverse Effect of BAL in a Case of Subacute Arsenical Polyneuritis, with Observations on Porphyrin Metabolism**
J. H. SANDS, B. BERRIS, and L. R. SCHERER. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 558–561, Oct. 12, 1950. 1 fig., 20 refs.

A case of arsenical polyneuritis in a man of 54 is described. The nerves chiefly involved were those of the lower limbs, and there were only slight signs in the arms. A trace of albumin and a few erythrocytes were found in the urine, but otherwise the only abnormality detected was a marked eosinophilia. Examination of the excreta and a muscle biopsy revealed no sign of parasites. After about 20 days in hospital the urine contained 1·12 mg. of arsenic in a 24-hour specimen and his hair 2·3 mg. per 100 g. Before admission he had drunk a considerable amount of whisky and this was shown to be contaminated with arsenious oxide to the extent of 150 mg. per 100 ml. About a fortnight later, in spite of the total delay of about 6 weeks since the ingestion of the arsenic, it was decided to try treatment with BAL, which was given in a dosage of 2·5 mg. per kg. per day, divided for 2 days into 6, and for 2 further days into 2, equal doses. After 4 days of treatment, however, the neurological signs were so aggravated that administration was stopped. Subsequently there was some slow improvement, but on the patient's discharge to another hospital 2 months later he had by no means recovered.

It is believed that this is the first case of arsenical

poisoning to be reported in which BAL has proved to be detrimental. It is suggested that the delay of 6 weeks before the treatment was instituted may have been at least partially responsible for this. Serial determinations of the urinary arsenic and coproporphyrin excretion were made. There was some, but only inconclusive, evidence that both were increased during the treatment with BAL. At all times, the urinary type-III coproporphyrin and the erythrocyte protoporphyrin contents were raised considerably above the normal level.

Reginald St. A. Heathcote

1414. **The Cerebrospinal Fluid in Methyl Alcohol Poisoning**

E. R. Reiner. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **64**, 528–535, Oct., 1950. 8 refs.

In 12 patients with methyl alcohol poisoning the cerebrospinal fluid pressure was raised to between 200 and 400 mm. of water in the first week, and to slightly lower values in the course of the subsequent 4 weeks. The increased pressure was not always manifested clinically. Repeated spinal punctures to remove excessive fluid were therapeutically effective, and were regarded as life-saving in some instances. The ocular signs and symptoms also were improved by these measures.

F. K. Taylor

1415. **Hyperglycaemia and Hypoglycaemia after Acute and Chronic Alcoholic Intoxication.** (Hiperglicemia e hipoglicemia conseqüentes à intoxicação aguda e crônica pelo álcool etílico)

D. Pfuhl Neves, C. Villela Faria, and T. Fujioka. *Revista do Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo* [*Rev. Hosp. Clin. Univ. S. Paulo*] **5**, 115–120, July, 1950. 4 refs.

Acute alcoholism may precipitate hypoglycaemia, an effect which has been attributed to substances other than alcohol contained in the drink, though this is unlikely. The patients affected are usually chronic alcoholics. Short clinical histories are given of 21 patients, the majority of whom were chronic alcoholics, who went into hypoglycaemic coma after 8 to 24 hours' fasting following an alcoholic bout; some of them had deficiency diseases such as pellagra. In addition 5 patients with no history of chronic alcoholism who suffered from hyperglycaemia of obscure origin are mentioned. The hypoglycaemic cases responded dramatically to the intravenous administration of glucose. The authors consider that the fall in blood sugar level is probably brought about by the toxic effect of alcohol on the liver, and is most likely to occur in " pre-cirrhotic hepatitis "—simple fasting does not cause hypoglycaemia. Ketonuria, on the other hand, is caused by fasting and not by acute alcoholism alone; thus whereas ketone bodies are usually absent from the urine in uncomplicated alcoholic coma they are often present in cases of hypoglycaemic coma in alcoholics. The authors stress the importance, from the point of view of therapy, of distinguishing between hyperglycaemic and alcoholic coma.

Paul B. Woolley

INDUSTRIAL TOXICOLOGY

1416. **Early Diagnosis of Plumbism.** (Tidlig-diagnostikk av blypåvirkning)

E. H. Schiøtz. *Tidsskrift for den Norske Lægeforening* [*Tidsskr. norske Lægeforen.*] **70**, 607–613, Oct. 1, 1950. 3 figs., 23 refs.

Under the auspices of the Oslo Factory Inspectorate, 1,096 workers exposed to lead were investigated. Taking punctate basophilia in more than 500 erythrocytes per million as abnormal, the author found 20% of those investigated were affected. Of 6 lead welders 3 had basophilia in more than 2,500 cells per million. High values were also obtained in workers employed in the accumulator industry, lead smelters, and fingerprint experts. The author has compared the results of the simpler basophil aggregation test with stippled-cell counts in 188 workers. There was reasonable agreement on the whole, but the former is not so reliable a test as the stippled-cell count carried out by highly trained personnel. The Inspectorate aims to remove from exposure to lead all workers with a punctate basophilia in more than 5,000 cells per million, as well as those in whom there is a sudden marked increase, regardless of the absence of clinical symptoms.

W. G. Harding

1417. **Effect of Exposure to the Vapors of Tetrabromoethane (Acetylene Tetrabromide): an Experimental Study**

M. G. Gray. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **2**, 407–419, Oct., 1950.

Tetrabromoethane has a specific gravity of 2·94 to 2·97 at 25° C., boils at 119° C. (15 mm. Hg), and decomposes above 242° C. These characteristics together with its chemical stability have led to its use as a substitute for mercury in gauges and balancing equipment. Inconsistencies in the literature suggested that a full investigation of the toxicity of tetrabromoethane was necessary.

Doses ranging from 0·25 to 0·5 g. per kg. of body weight were administered by stomach tube to guinea-pigs and rabbits. The LD 50 for both species was found to be 0·4 g. per kg. In the animals which died there was a latent period of 12 to 24 hours before symptoms of narcosis appeared, and death occurred in 2 to 4 days after a period of coma. At necropsy the liver and kidneys were pale and the lungs showed haemorrhagic changes. Inhalation experiments were carried out in a gas chamber of 1 cubic yard (0·764 c.m.) capacity under controlled conditions of temperature and humidity. Tetrabromoethane was poured into a tray at the bottom of the chamber under a wire-mesh floor, and the vapour arising was circulated by an electric fan, a rough check being made to verify that the atmosphere within the chamber was saturated with vapour. The oxygen content of the chamber was shown to be sufficient for normal respiration during the period of the experiment. Rabbits, rats, and guinea-pigs showed no ill effects after a single exposure of 2 hours, apart from some respiratory irritation, but 2 to 3 hours' exposure resulted in ataxia and unconsciousness. After removal from the chamber

the rabbits and rats recovered in 24 hours. The guinea-pigs, however, died within 1 to 5 days and necropsy showed fatty changes in the liver and kidneys. Necropsy of the surviving animals showed no such changes. Guinea-pigs, mice, and rats were exposed to saturated atmospheres of tetrabromoethane for 15 minutes daily for 47 to 92 days. Rabbits obtained an additional oral dose by licking the condensed vapour from the sides of the cage and for this reason were eliminated after the first experiments. No ill-effects were observed either during or after exposure, and no cumulative effect was discovered.

On decomposition tetrabromoethane forms bromine, hydrobromic acid, and other products. Exposure to these decomposition products was fatal to rats and rabbits. A saturated atmosphere of tetrabromoethane was shown to be less toxic than 2·25% by volume of methyl chloride. *W. K. S. Moore*

1418. **Comparative Acute and Subacute Toxicities of Allethrin and Pyrethrins**

C. P. CARPENTER, C. S. WEIL, U. C. POZZANI, and H. F. SMYTH. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **2**, 420–432, Oct., 1950. 4 refs.

Allethrin is the allyl homologue of cinerin I and possesses insecticidal properties comparable with those of the natural pyrethrins. Toxicity tests were carried out with aerosol bombs containing 1% of the insecticide under test, 9% peanut oil, and 90% " freon 12 " (propellant). In control bombs the insecticide was omitted. Exposures lasted 30 minutes and were carried out in chambers of 20 c. ft. (0·566 c. m.) capacity, concentrations in the region of 50 g. of aerosol mixture per 1,000 c. ft. (1·768 g. per c.m.) being used, this being about 10 times the concentration used in treating aircraft.

No ill effects were noticed when rats were exposed for 85 periods of 30 minutes in 67 days to laboratory produced allethrin, commercial allethrin, pyrethrum, or the control peanut-oil aerosols. Dogs were also unaffected after receiving 40 exposures during 26 days. When the aerosol concentration in the chamber was increased to between 16,700 and 18,500 g. per 1,000 c. ft. (590 to 654 g. per c.m.) and rats exposed for 30 minutes there were still no ill effects. The use of a nebulizer allowed the concentration to be increased still further. One out of 10 rats died after being exposed to a concentration of 19 mg. of commercial allethrin per c.m. for 2 hours, while 4 out of 10 died after 4 hours' exposure to a concentration of 13·8 mg. per c.m. The main pathological findings in these animals was cloudy swelling in the liver and renal tubules. The acute oral LD 50 for rats of both commercial allethrin and pyrethrin was found to be about 1 g. per kg. Allethrin was found to be non-irritant to the cornea, and practically non-irritant to the skin of rabbits. Skin sensitization could not be produced.

In general, therefore, commercial allethrin was found to be of the same order of toxicity as the pyrethrins, and could be used just as safely as an insecticide in sprays and aerosols. *W. K. S. Moore*

1419. **Chronic Oral Toxicities of Mercuri-phenyl and Mercuric Salts**

O. G. FITZHUGH, A. A. NELSON, E. P. LAUG, and F. M. KUNZE. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **2**, 433–442, Oct., 1950. 2 figs., 1 ref.

Phenylmercuric acetate and mercuric acetate were added to a basic diet to give concentrations of 0·1, 0·5, 2·5, 10, 40, and 160 p.p.m. of mercury, and groups of at least 20 rats were fed on each of the resultant diets, two control groups being given the basic diet alone. Apart from 2 animals from each group which were killed after one year, all the rats continued on their allotted diet for the full life-span. The additions to the basic diet did not affect the food consumption of any group, but there was depression of growth in all rats receiving more than 40 p.p.m. of mercury as phenylmercuric acetate, while in the males, which were more susceptible, this depression occurred even with 10 p.p.m. Mercuric acetate had little effect on growth even at concentrations of 160 p.p.m. of mercury. The kidneys were significantly enlarged after ingestion of 40 and 160 p.p.m. of mercury in either form, the liver being slightly heavier than in the controls, though not significantly so, at the same dosage levels. Chemical analysis of these organs showed that considerably more phenylmercuric acetate was stored than mercuric acetate (estimated as mercury). The content of mercury in the urine after the ingestion of the organic salt was also very much higher than in the case of mercuric acetate. It is concluded that the former is absorbed more rapidly from the intestine than the latter.

At necropsy the gross changes associated with ingestion of mercury were granularity, fibrosis, and enlargement of the kidney, pallor of the viscera, and hair balls in the stomach. The renal changes occurred in all groups, including the controls, but were most marked in the animals which had received phenylmercuric acetate and least in the control group. The principal microscopic lesion observed in the kidneys was dilatation and cyst and cast formation in the proximal convoluted tubule, with secondary fibrosis. It was noticed that the same type of change occurred in all groups of rats, but the damage was most marked where the organic salt had been given, less marked after the inorganic salt, and least in the controls. It appeared that ingestion of mercury merely hastened a normal degeneration process.

[The strain of rat used is not mentioned, and no reference is made to previous observations of the renal changes described as occurring in the control groups.] *W. K. S. Moore*

1420. **Paranoid States Occurring in Leaded-petrol Handlers**

V. L. KAHAN. *The Journal of Mental Science* [*J. ment. Sci.*] **96**, 1043–1047, Oct., 1950. 3 refs.

The author describes 6 cases of paranoidal states associated with lead poisoning in Indian males who were seen at Basra in 1943. These men had worked for periods ranging from 3 months to 2 years for long shifts in enclosed spaces filled with a heavy concentration of fumes from petrol to which tetraethyl lead had been added.

The chief symptoms consisted of acute excitement, confusion, hypochondriasis, fears, insomnia, and emaciation. Two patients died. Punctate haemorrhages were found throughout the hemispheres in one case and demyelination of the pontine nerve bundles in both cases. One patient improved without active treatment; 3 others improved under treatment consisting of the administration of magnesium sulphate intravenously and an alkaline mixture by mouth.

G. de M. Rudolf

THERAPEUTICS

1421. **Protein Metabolism in Chronic Illness: Effect of Protein Supplementation on Nitrogen Balance, Hemoglobin, Serum Proteins, and Weight in the Malnourished and the Effect of the Nutritional Status on Nitrogen Storage**
S. O. WAIFE, M. G. WOHL, and J. G. REINHOLD. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 604–616, Oct., 1950. 5 figs., 36 refs.

The subjects of the investigation here reported were 12 hospital patients, of whom 10 had diabetes mellitus associated with a complication (usually gangrene or cellulitis), one had severe atypical anaemia, and one had rheumatoid arthritis. All the subjects had either hypoalbuminaemia (with a serum albumin level of less than 4·0 g. per 100 ml.) or were "malnourished" clinically, with a low-normal serum albumin level. All the patients had previously been receiving a hospital diet in which the protein constituent (11 to 14 g. of nitrogen daily) was presumably adequate, and all were found to be in nitrogen equilibrium, or with a slightly positive balance, during a preliminary control period. A casein concentrate was then given orally to 10 patients in amounts which represented a 100% addition of protein to the usual diet; one patient received only 4 g. of additional nitrogen daily, and one who received no protein supplement served as a control. The nitrogen balance was studied for an average period of 50 days.

In 6 of the 10 patients who received a 100% supplement of protein the positive nitrogen balance was proportional to the additional nitrogen intake, the patients being able to store about three-quarters of the supplementary protein; in the remaining 4 patients the nitrogen balance increased only slightly. There was no apparent differentiation clinically between the two groups, except that among the diabetics the disease was more severe in the former group as shown by the greater amount of insulin required. The changes in serum albumin and serum globulin levels were not correlated with the amount or the rate of nitrogen storage. There was a significantly greater rise in haemoglobin level in the former group, but this was significantly greater in those members of the group with the lower rates of nitrogen storage. The former group gained more weight than the latter group, but changes in weight were not consistently correlated with the amount of nitrogen stored: "a surprising finding was the large amount of nitrogen storage and presumably tissue rebuilding without parallel weight change."

The former group, it is suggested, were in a more severe state of "protein-depletion", and their avidity for protein may have resulted from their protein metabolism having passed [when?] from a catabolic to an anabolic phase through the "stress" of illness. [What, even in broad terms, was the particular stress? Presumably what is meant is some deterioration in the course of the chronic illness or some acute complication. One is unable to judge from the sparse clinical data whether or not this is likely to have been a factor during the period of investigation. The finding of nitrogen equilibrium during the preliminary control periods would not, *per se*, necessarily support or disprove this theory.] It is suggested that "further work is needed to distinguish this group in order to avoid useless and indiscriminate protein supplementation."

[Although the authors' theoretical interpretation is vague, the actual findings are interesting and important.]

Joseph Parness

1422. **Effect of Intravenous Injection of Typhoid Vaccine on Blood Leukocytes and Adrenal Cortex**
M. D. ALTSCHULE, B. H. PARKHURST, and E. PROMISEL. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 505–518, Oct., 1950. 7 figs., 42 refs.

Observations were made on 6 patients receiving intravenous injections of typhoid vaccine for the treatment of various psychoses. The number of circulating eosinophils, which was initially normal in every case, had fallen by 54 to 97% (average 80%) 4 hours after the vaccine was given. The same degree of fall in eosinophil count was observed after each subsequent injection and was not influenced by the severity of the febrile reaction. The lymphocyte count, which was initially normal in all cases, also fell, by 35 to 92% (average 75%), after each injection, there being a linear relation between the initial count and the degree of fall. The granulocyte count rose after the injection in all cases, usually increasing by 50 to 200%. The urinary uric acid : creatinine ratio ranged from 0·22 to 0·36 before injection and rose markedly (by 50 to 200%) after each injection in 11 out of 16 cases studied, there being an inverse relation between the degree of elevation of temperature and the degree of change in this ratio.

The changes in eosinophil and lymphocyte counts and uric acid : creatinine ratio were less marked in response to electric-shock therapy and became progressively less with successive treatments; they were still smaller in patients who had previously received fever therapy. This suggested to the authors that adrenocortical response was not the only factor involved, but that there might also be some toxic or immunological factor at work.

Robert de Mowbray

1423. **The Favourable Effect of Phenothiazine Derivatives on the Preservation of Blood.** (Influence favorable sur la conservation du sang des dérivés de la phénothiazine)
B. N. HALPERN, B. DREYFUS, and G. BOURDON. *Presse Médicale* [*Pr. méd.*] **58**, 1151–1153, Oct. 18, 1950. 8 figs., 11 refs.

Various quantities of certain derivatives of phenothiazine ("antergan")—mepyramine ("neoantergan"), "3015 RP", promethazine ("phenergan"), "3300 RP",

diethazine (" diparcol "), and " parsidol "—were added to blood diluted with Wurmser's solution (citric acid 3%, sodium hydroxide 1%) in the proportion of 1 volume of the latter to 4 of the former, the mixture being stored in a refrigerator. The state of preservation of the erythrocytes was judged by the degree of haemolysis, the plasma potassium level, total erythrocyte volume on sedimentation after agitation, morphology of the erythrocytes, and haematocrit reading. That of the leucocytes was judged by their morphology (May–Grünwald–Giemsa staining) and phagocytic activity. Promethazine and 3300 RP in dilutions of 1 in 10,000 to 1 in 20,000 were the only effective preservative agents. The authors presume that the action of these substances lies in their inhibiting effect on certain unspecified enzymes.

Harold Caplan

1424. **Blood Exchange in Replacement Transfusions. II. Studies with Erythrocytes Tagged with Radio-active Phosphorus**

L. R. WASSERMAN, I. A. RASHKOFF, L. SHARNEY, T. F. YOH, and D. LEAVITT. *Blood* [*Blood*] **5**, 938–949, Oct., 1950. 6 figs., 12 refs.

1425. **Intermittent Treatment of Poliomyelitis with Progressive Resistance Exercise**

S. MEAD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 458–460, Oct. 7, 1950. 6 figs., 8 refs.

The treatment described by the author is designed to hypertrophy muscles and parts of muscles that still retain their nerve supply. In this treatment, which was first used by de Lorme, an elaborate table with counterbalances is employed which can, if necessary, take the whole body weight. The author plots his results graphically and is thus able to tell the point beyond which no further improvement in the hypertrophy of a particular muscle is likely. He believes in treating patients intensively for 3 weeks, then sending them home for 3 or 4 months before a further 3 weeks' treatment.

G. S. Crockett

1426. **Suspension Kinesitherapy**

O. F. VON WERSSOWETZ and C. W. PAINTER. *Occupational Therapy and Rehabilitation* [*Occup. Therap.*] **29**, 265–274, Oct., 1950. 8 figs., 8 refs.

The authors recommend the use of suspension kinesitherapy in the re-education of weakened and paralysed muscles, suspension permitting movements to be activated by momentum and thus requiring the minimum of muscular effort from the patient. The apparatus used is a modification of the Guthrie–Smith suspension frame. They give three main guides to the selection of fixation points on the support frame for suspension of the limb in so far as the resulting movement arc is concerned: (1) Using a point of fixation vertically above the joint a horizontal movement is obtained. Such swing allows for maximum range of motion with minimum resistance or assistance. (2) With the point of fixation vertical to the bodily segment but at any position other than perpendicular to the joint a pendulum swing will be obtained which will be governed by laws of simple periodic motion. (3) With any point of fixation other than vertical to the bodily segment the movement arc will be a phase of pendulum swing so that a given muscle group may be assisted or resisted.

In an attempt to assess the efficacy of suspension therapy the authors have analysed the progress in 184 consecutive cases of different conditions, and report good results in 61·8%, moderate results in 29·4%, and poor results in 8·8%. Further controlled studies are being conducted and will be reported later.

M. H. L. Desmarais

INSECTICIDES

1427. **A Critical Evaluation of DDT and " Gammexane " in Malaria Control in Upper Assam over Five Years, with Particular Reference to their Effect on *Anopheles minimus***

D. M. BERTRAM. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **44**, 242–254, Oct., 1950. 5 figs., 7 refs.

The observations recorded in this paper represent a continuation of the work initiated by Ribbands (*Bull. ent. Res.*, 1947, **37**, 567). They describe the results obtained with residual sprays of DDT and " gammexane ", in the form of solutions, emulsions, and suspensions, against the adult forms of *Anopheles minimus* entering native huts on tea-estates in Upper Assam, where this species is the principal vector of malaria.

The present author claims that these results justify the belief that " for the control of malaria transmitted by *A. minimus*, DDT can be no more recommended than it can for the control of malaria transmitted by *A. gambiae*. Gammexane is obviously to be preferred. This demonstration that DDT excitation or repellency is not confined to *A. gambiae* strongly suggests that similar tests should be carried out on all known malaria vectors."

[This paper contains much information which does not lend itself to summarization, and should be consulted in the original by those interested.] *R. M. Gordon*

1428. **Larvicidal Treatments with DDT and " Gammexine " in Upper Assam, with Particular Reference to their Effect on *Anopheles minimus***

D. M. BERTRAM. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **44**, 255–259, Oct., 1950. 1 ref.

Anopheles minimus is a flowing-water breeder, and on certain tea-estates in Upper Assam the larvae of this species occur in such inaccessible sites in the rivers as to render ordinary biological control an uneconomical procedure. Under these circumstances, 5% DDT in malariol, or 2% " gammexane" liquid concentrate L.G. 140, produced excellent, and apparently equally good, results when applied in previously calculated dosages. For the larvicidal treatment of still water gammexane L.G. 140 proved more potent than DDT.

R. M. Gordon

Medical Jurisprudence

1429. **Some Observations on a Case of Dementia Consecutive upon Strangulation**
B. KRAFT. *Folia Psychiatrica, Neurologica et Neurochirurgica Neerlandica* [*Folia psychiat., Amst.*] **53**, 535–548, Aug., 1950. 29 refs.

A boy of 15 years was found by his father suspended by the neck between two strands of a clothes line stretched across a shed. He was deeply comatose and cyanosed, and the pulse was just palpable. He was removed to hospital where he remained unconscious for 2 days. He had paresis of the legs, but this disappeared 4 days later. The psychic state of the boy was found to have changed after the accident. He did not speak and was incontinent. He was discharged in this condition. Three years later he was re-admitted because his mental condition had not improved. At this time the boy was very restless, could not speak, laughed in a neighing fashion, had to be fed, and was incontinent; contact could only be established with him in a transitory way. He had no convulsions and he could probably recognize his mother. His mental development was that of a child of from 1 year to 18 months old. No change occurred in his condition while in hospital, and he was taken home.

The author considers whether the case was one of suicide or accident, and concludes that there is no evidence to point to suicide. He describes several reported cases of child suicide by hanging, and points out that in the U.S.A. between 30 and 55 children under 14 years of age commit suicide annually, a high proportion of them selecting hanging as the method. In typical hanging the nasopharynx is occluded, the arteries and veins to the head are compressed, and the vagus may be stimulated and cause reflex inhibition of the heart. The present case is atypical, because only the sides of the neck were compressed. Direct asphyxia is, therefore, ruled out, the pressure on the cervical vessels being the important factor. The protracted cerebral anaemia thus resulting produced irreversible changes in the brain, causing grave and permanent deterioration of the intellect amounting to dementia. The author draws a parallel between the sequelae in this case and those which may occur after carbon monoxide poisoning and severe concussion. *Gilbert Forbes*

1430. **The Diagnosis of Uraemia in the Cadaver.** (La diagnosi di uremia nel cadavere)
F. TARSITANO. *Folia Medica* [*Folia med., Napoli*] **32**, 310–318, July 7, 1950. 6 refs.

In a small series of cases of death from both non-renal and renal causes a study was made of the blood urea level in the cadaver, blood being taken from the left ventricle and the hypobromite method used for estimation. In the former group, in all of which the kidneys were found to be normal, a post-mortem rise in blood urea content occurred, but the maximum level remained within normal limits, ranging from 47 to 126 mg. per 100 ml., the figures being slightly lower in cases of sudden death. The values in the renal group were much higher, ranging from 270 to 340 mg. per 100 ml. In addition the blood urea levels in 4 dogs during the agonal period and after death were compared, the post-mortem increase varying between 8 and 35 mg. per 100 ml. It is pointed out that this post-mortem rise is independent of the state of preservation of the body. The author concludes that the diagnosis of uraemia can only be made safely post mortem when the blood urea level is considerably in excess of normal. *G. J. Cunningham*

1431. **Observations on Seminal Stains**
S. D. S. GREVAL, D. K. GHOSHAL, and B. C. DAS. *Indian Journal of Medical Research* [*Indian J. med. Res.*] **38**, 83–88, Jan., 1950. 6 figs., 19 refs.

The authors point out that morphological description of the human spermatozoon as consisting of head, neck, and tail, given in most textbooks of forensic medicine, is inaccurate, it being more correct to speak of it as consisting of a head, a body or middle-piece, and a tail.

Florence's reagent (iodine 2·5 g., potassium iodide 1·65 g., and water 30 ml.) is generally used in the routine examination of stains suspected of being seminal. The clothing or other material to be examined is soaked in saline or, preferably, Vibert's fluid (sodium chloride 2 g., mercuric chloride 0·5 g., water 100 ml.) for 30 minutes. It is then dabbed on to a microscope slide, covered, and the reagent run in under the cover slip. Dark brown rhomboid crystals are seen in positive cases, and tend to disappear leaving an oily residue. They are not diagnostic, and stained spermatozoa must be seen for a positive report to be given. Under tropical conditions the picric acid test (with saturated solution of picric acid in alcohol or water) is not of great value, even though crystals of spermine picrate may be seen.
P. N. Meenan

1432. **Carbon Monoxide Poisoning. Accident, Suicide and Murder**
F. E. CAMPS. *Medico-Legal Journal* [*Med.-leg. J.*] **18**, 75–85, 1950.

Coal gas contains from 5 to 22% of carbon monoxide, for which haemoglobin has an affinity 300 times greater than for oxygen. Hence a small percentage of coal gas in the inspired air may give rise to a fatal concentration of carbon monoxide in the blood, given time. The author reviews the circumstantial evidence which may serve to place individual cases of death from coal-gas poisoning in the correct category of accident, suicide, or homicide, and gives a number of illustrations. The difficulty of unravelling apparent suicide pacts is stressed, and the possibility of a murder being arranged to look like suicide is emphasized. An important point mentioned is that amnesia may be a sequel to sublethal carbon monoxide poisoning. *Gilbert Forbes*

Radiology

1433. **Platelet Values in Personnel Engaged in Roentgen Diagnostic Work.** [In English]
H. MOSSBERG. *Acta Radiologica* [*Acta radiol., Stockh.*] **34**, 186–192, Sept., 1950. 1 fig., 6 refs.

The author has investigated the platelet counts of 24 persons working in a diagnostic *x*-ray department. The counts were carried out by a modified Kristenson method which is described. In a control series of 16 persons not engaged in radiological work the counts were found to fall between 300,000 and 200,000 per c.mm. The counts of the *x*-ray workers fell between just over 200,000 and 130,000 per c.mm. The findings were regarded as significant of radiation damage to the haematopoietic system in about one-third of those examined, their count being less than 150,000 per c.mm. Rather more than one-third were regarded as possibly suffering from radiation damage, their count being below 200,000 but above 150,000 per c.mm.

In view of the fact that the platelet count is in general very stable and less influenced by transient factors such as infections or allergy than is the leucocyte count, and in spite of the fact that it is rather more difficult to carry out with accuracy, the author urges that the platelet count be adopted as a routine index of radiation effect in *x*-ray workers. *A. M. Rackow*

1434. **Electrokymographical Studies of Coarctation of the Aorta.** [In English]
S. R. KJELLBERG and U. RUDHE. *Acta Radiologica* [*Acta radiol., Stockh.*] **34**, 145–153, Sept., 1950. 6 figs., 16 refs.

Studies were made of the electrokymograph tracings in 12 patients with coarctation of the aorta, comparing these with normal electrokymograms. Readings were made of points on the ascending aorta and at other points lying distal to the site of stenosis. All the cases had been confirmed by clinical and angiocardiographic evidence as being of coarctation.

The electrokymogram in a case of coarctation, when made distal to the stenosis, is characteristic. The curve rises very slowly and there is absence or diminution of the secondary curve caused by closure of the semi-lunar valves. The whole curve has a smoother and more sinusoidal character than in the normal subject. Five of the cases are described in detail and the curves reproduced. *A. M. Rackow*

1435. **Impulse Radiography of the Heart and Great Vessels.** (Импульсная рентгенография сердца и крупных сосудов)
E. A. LIKHTENSHTEJN and M. F. POPOV. Клиническая Медицина [*Klin. Med., Mosk.*] **28**, No. 10, 36–40, Oct., 1940. 2 figs.

This paper stresses the advantages of instantaneous radiography of the heart and large vessels. Rapid exposures are achieved by means of a condensor *x*-ray generator, which is capable of exposures of 0·01 to 0·05 second. Such rapid exposures have been particularly useful for the delineation of the heart and large vessels in cardio-angiography with opaque substances and for differentiation between the shadows of the heart and closely adjoining pathological tissues, such as cysts or solid tumours.

[*X*-ray condensor plants were in limited use in Great Britain and in Germany for a short time in the early thirties. They were introduced mainly to overcome the difficulties of weak and erratic electric supplies. The modern *x*-ray generator with the rotating anode tube can accomplish all that the condensor plant did and much more besides. The authors of the paper speak of the condensor plant as of something entirely new invented by themselves.] *A. Orley*

1436. **Amplifying and Intensifying the Fluoroscopic Image by Means of a Scanning *X*-ray Tube**
R. J. MOON. *Science* [*Science*] **112**, 389–395, Oct. 6, 1950. 3 figs., 3 refs.

1437. **The Traveling-wave Linear Accelerator**
E. R. WIBLIN. *Science* [*Science*] **112**, 399–400, Oct. 6, 1950.

RADIOTHERAPY

1438. **I^{131} in the Diagnosis and Treatment of Hyperthyroidism**
R. A. SHIPLEY, J. P. STORAASLI, H. L. FRIEDELL, and A. M. POTTS. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 576–589, Oct., 1950. 3 figs., 18 refs.

The use of radioactive iodine (^{131}I) in the diagnosis and treatment of hyperthyroidism in a series of 29 cases of diffuse and 18 of nodular goitre is reported. Various methods of demonstrating, for diagnostic purposes, the increased uptake of ^{131}I which occurs in this disease are described and it is concluded that the most suitable method for use in everyday practice is the indirect determination of the total retention of a dose of ^{131}I by measurement of the urinary excretion in a single 48-hour urine specimen, rather than the determination of the "collection rate", as suggested by Keating, or the employment of direct measurement over the thyroid. In the series of cases under discussion two consecutive 24-hour specimens were collected, it being originally intended to observe the effect of increased thyroid activity on the ratio of the radioactivity of the two samples, the greater activity usually being found in the first specimen in hyperthyroidism and in the second in myxoedema. Statistically, however, determination of

the ratio was not shown to be more useful than that of total retention by assay of the single 48-hour specimen. By the latter method a definite difference in result was found as between hyperthyroidism, euthyroidism, and hypothyroidism, although there was considerable overlap between the different groups.

In the treatment of patients with ^{131}I the dose was related to the amount of ^{130}I previously used and was estimated in microcuries of retained ^{131}I per g. of gland. Retention was estimated by means of a tracer dose and gland size by clinical examination. The mean dose of ^{131}I administered (without correction for retention) was 7 millicuries in cases of diffuse goitre and 13·2 in those of nodular goitre, the mean calculated doses to the gland being 95 and 135 microcuries per g. respectively. Myxoedema occurred in 4 cases of diffuse goitre, but in none of nodular goitre. Six weeks elapsed before clinical improvement or change in size of the gland was observed and the maximum improvement had usually occurred by 3 months. There was no improvement in exophthalmos on the whole and, as after thyroidectomy, there was sometimes temporary exacerbation. Little local discomfort was experienced. Two interesting points noted were the apparent resistance of nodular goitre to overdosage and the fact that there seemed to be little difference between the dosage causing myxoedema and that having no effect. It is suggested that uptake of ^{131}I in the goitre is uneven and that this may explain the resistance of nodular goitre to overdosage, Such unevenness of uptake has been demonstrated in autoradiographs.

V. M. Dalley

1339. **A Case of Squamous Epithelioma of the Tongue in a Young Woman, aged Nineteen Years**

R. Flynn and H. Harris. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 548–549, Oct. 7, 1950. 2 figs.

The authors report the case of a girl who had a carcinoma of the tongue at the age of 19 and is alive and well nearly 10 years later. When first seen she had an eight weeks' history of a tumour which had grown to form an ulcer 1 inch (2·5 cm.) in diameter on the infralingual surface on the left side, 1½ inches (3·75 cm.) from the tip. The Wassermann reaction was negative. A biopsy specimen showed squamous-celled carcinoma. Radium needles were inserted into the tongue and 2 months later, when bilateral nodes became palpable, bilateral block dissection of the neck was carried out. Several nodes were found to be invaded by carcinoma on the left side, but there was no evidence of involvement on the right. After operation *x*-ray therapy was given to the left side.

D. Waldron Smithers

1440. **The Use of Radioactive Phosphorus in the Treatment of Carcinoma of the Breasts with Widespread Metastases to Bone**

H. L. Friedell and J. P. Storaasli. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 559–575, Oct., 1950. 9 figs., 16 refs.

The authors record their experience in the treatment of carcinoma of the breast with widespread bone metastases by means of radioactive phosphorus (^{32}P). The work was initiated in 1942 by the treatment of a woman, aged 47, who had had a radical mastectomy in 1937 and had since developed widespread bone metastases. In February, 1942, she received 20 mc. of ^{32}P in one month, given in two 1-mc. doses at regular intervals. Six weeks later the erythrocyte and leucocyte counts were found to be considerably reduced, but responded to blood transfusion and other measures. One year later the disease appeared to have been arrested, some bone regeneration had occurred, and the blood picture was normal. In September, 1944, on recurrence of symptoms, 9·4 mc. of ^{32}P was given in 24 days, with subsequent blood changes as before. After a 2-year remission the disease recurred, and in January, 1947, 9·4 mc. was given in 37 days. (The results were obscured by testosterone treatment given at same time.) Death occurred in 1948 in the presence of widespread disease. The rationale of the use of ^{32}P in such cases (which is based mainly on the differential absorption rate of phosphorus by rapidly growing tissues compared with normal adult tissues) and the factors affecting its deposition in the body are discussed and its physical characteristics described.

Since 1942, the authors have treated 12 patients, the criteria for selection being histological proof of carcinoma of the breast and the presence of widespread bone metastases causing severe pain. Dosage was based on previous experience, but in general 3 mc. per 10 kg. body weight was given in 2-mc. doses at 5-day intervals; the average total dose was 18·2 mc. in 40 days. There was usually definite relief of pain and occasionally some recalcification, but no evidence of increased longevity among the patients treated. The main complication was depression of marrow activity. Cessation of menstruation occurred in 2 of the 3 pre-menopausal patients. Autoradiographs of necropsy material in 6 cases showed that there had been selective uptake of ^{32}P by tumour tissue, and in one case the relative uptake by the various organs was assayed. An attempt is made to calculate the dosage received by the bones in this method of treatment. [In the subsequent discussion it was agreed by the authors that the treatment was experimental and had little obvious superiority to other forms of treatment.]

V. M. Dalley

1441. **The Treatment of Polycythaemia with Radioactive Phosphorus.** (Traitement de la maladie de Vaquez par le radiophosphore)

J. Closon. *Presse Médicale* [*Pr. Méd.*] **58**, 1192–1195, Oct. 25, 1950. 5 figs., 39 refs.

1442. **Radiotherapy of Osteosarcoma of the Long Bones in Young Subjects.** (La roentgenthérapie dans les ostéosarcomes des os longs chez les sujets jeunes)

F. Baclesse and G. Herlory. *Presse Médicale* [*Pr. méd.*] **58**, 1075–1076, Oct. 4, 1950. 7 figs.

Biopsies were carried out in 9 cases of osteosarcoma treated primarily with deep *x* rays from 1936 to 1947. There were 6 cases of osteogenic, 1 of fibro-, and 2 of osteochondromyxo-sarcoma; 8 were of the femur, 1 of the tibia. Of 6 patients who had *x*-ray treatment only, 4 died rapidly of metastases and 2 survive and, after 14

and 3 years respectively, are clinically cured. The other 3, after primary irradiation, had to undergo disarticulation for late trophic radiation effects on the tissues; one of these 3 died with metastases, but the other 2 are alive and well 8 years after irradiation and 3½ and nearly 3 years respectively after operation. The first of the 2 operation specimens, though clinically and radiologically there had been no evidence of activity, was found to be fully active histologically; in the other case the pathologists disagreed as to whether residual activity or sterilization of growth was shown. The behaviour of these growths is seen to be variable and unpredictable from clinical and radiological evidence.

Treatment was given to 4 long, narrow fields all round the limb with a dosage of 150 to 200 r per field and an interval usually of 2 days between doses to the same field. The skin dose did not exceed 4,000 r. The respective tumour doses in the 4 long-term survivors were 9,100 r, 9,200 r (no surgery), 6,500 r, and 8,500 r (later surgery). Stress is laid on the importance not only of high total dosage, but also of prolonged fractionation to avoid late radiation damage. The patient treated with 9,100 r showed late tissue changes, whereas the patient given 9,200 r did not, since the over-all treatment time was greater. Treatment in a single course is possible, but it is considered preferable to split it up into 2 or 3 periods at intervals of 2 to 3 months. Moist desquamation of the skin must be avoided. It is concluded that with high-dosage, protracted *x*-irradiation it is possible to arrest the growth of these tumours at least temporarily, and possibly permanently.

J. Walter

1443. **By-effects of Irradiation on the Skin**
A. W. STILLIANS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 743–746, Oct., 28 1950. 4 figs., 7 refs.

This paper from Chicago starts with a short review of the irradiation effects of ultraviolet light and *x* rays on the skin, including tanning and burning, infectious eczematoid dermatitis, comedos, and erythema multiforme; particular interest centres on tumour formation, which has been reported in cases of senile keratosis exposed to strong sunlight and in cases of cancer subjected to *x* rays. There is a report of a case of senile keratosis with a fine elevated line at one border of the keratosis, like that commonly present on erythematoid epitheliomata. The skin was liable to inflammatory reactions on exposure to strong sunlight. The lesion was treated on two occasions at an interval of 3 days with 3 erythema doses of radiation from a plaque of radium screened with 0·1 mm. of aluminium at 2 mm. distance: 5 weeks later a nodule was seen at the edge of the keratotic area, which had reddened, oozed, and crusted following the treatment. The nodule disappeared within 3 weeks. The histological features of a punch-biopsy specimen are discussed: they are those of an inflammatory reaction of an extremely acute fibrinous type. Various hypotheses regarding the cause of the nodule are considered by the author, who favours the opinion that it is an uncommon early radiation effect, though he also states that strong light is a factor in these cases. The histologist, on account of the absence of characteristic epidermal and vascular changes of acute *x*-ray dermatitis, does not agree that irradiation is implicated.

Edward M. McGirr

1444. **Intracavitary Visceral Radiation: Effect on Gastric Acid Secretion**
J. B. R. MCKENDRY. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 25–27, Oct., 1950. 3 figs., 6 refs.

A simple and ingenious device for intracavitary irradiation of the stomach is described. Two thin-walled, concentric, rubber bags are cemented together in their proximal two-thirds with about one dot of cement per sq. cm. of surface of the distended bag, while in the distal one-third the two layers are completely cemented together. In this way a balloon having an intramural cavity with a capacity of about 10 ml. is produced. This is filled with a solution containing radioactive iodine (^{131}I) which emits beta rays of fairly high energy. The bag is passed attached to a 2- or 3-lumen Miller–Abbott tube. So far only animals have been irradiated by this means, achlorhydria having been successfully induced in several dogs without evident damage to their health.

[The abstracter has previously expressed his doubts as to whether this form of treatment for peptic ulcer is either theoretically sound or safe.]

Denys Jennings

1445. **Diagnosis and Treatment of Brill–Symmers Disease.** (Clinica e terapie del linfoblastoma gigantofollicolare. (Malattia di Brill–Symmers))
U. COCCHI. *Radiologia Medica* [*Radiol. med., Torino*] **36**, 705–713, Sept., 1950. 4 figs., 23 refs.

Since this disease was first described 25 years ago by Brill and Symmers, some 200 cases have been reported. Clinically, the disease is characterized by more or less generalized lymph-node enlargement, frequently associated with splenomegaly (55% of cases) and sometimes with hepatomegaly (15%). The nodes most frequently affected are the cervical, supraclavicular, axillary, and inguinal. In some cases there are also pleural effusion, ascites, exophthalmos, and cutaneous and osseous changes. The patient's general condition remains good for quite a long time, but in the terminal stages of the disease cachexia supervenes. There may be a moderate leucopenia, with lymphocytosis or lymphopenia, but the blood picture may also be completely normal. Anaemia is rare and the erythrocyte sedimentation rate is normal or somewhat increased. The age incidence is between 30 and 60, with a slight preponderance of males (59%). The diagnosis can be established only by the histological examination of the nodes, the characteristic finding being of giant polymorphous lymphoid cells with numerous mitoses. In the majority of the cases reported in the literature the patient died about 3 years after the first hospital attendance, but some patients have survived as long as 5, 7, or even 10 years. In 17% of cases sarcomatous changes eventually developed. Treatment may be with surgery, radiotherapy, or chemotherapy, or with combinations of these: the lesions show considerable

radiosensitivity. The average survival in untreated cases amongst those reported was 2 years, 11 months, and in treated cases 4 years, 6 months. No case of spontaneous cure has been recorded.

The author here reports 5 new cases of the disease recently observed at the Institute of Radiotherapy of the University of Zürich and treated with combined radiotherapy and chemotherapy. Two of the patients are still under treatment, 2 have died (one of reticulosarcoma which developed after 6 years' intermittent treatment), and one patient has been completely free from signs and symptoms for 3 years since the last treatment. The degree of radiosensitivity of this disease is so great that the affected lymph nodes disappear completely and for a long time after irradiation with a dose as small as 400 r. However, a certain degree of radioresistance develops after repeated radiotherapy, and the author therefore recommends much larger initial doses than may appear necessary (minimum 3,500 to 4,000 r). In the author's experience the results of chemotherapy with nitrogen mustard have, on the whole, been good, although side-effects were frequent. He is of the opinion, however, that chemotherapy (which is still in the experimental stage) should be reserved for cases in which the disease is generalized until such time as its value can be more accurately assessed. In the meantime, the routine treatment for all cases of Brill–Symmers disease should be with radiotherapy. *L. G. Capra*

1446. **Intracavitary Radium at Time of Vaginal Plastic Operation**
L. L. Weber. *American Journal of Obstetrics and Gynecology* [*Amer. J. Obstet. Gynec.*] **60**, 371–378, Aug., 1950. 2 figs., 6 refs.

The author reports 131 consecutive cases, seen at the Mount Sinai Hospital from 1928 to 1947, in which repair of the vagina was carried out simultaneously with the application of intra-uterine radium for benign disease. The average age of the patients was 45·5 years. Of the total number 108 complained of abnormal uterine bleeding in addition to symptoms referable to prolapse. On histological examination 87% of the cervical specimens available showed chronic cystic cervicitis; this, together with the abnormal bleeding in women of this age, may be to most gynaecologists an indication for vaginal hysterectomy. Only 76 of the endometrial specimens removed by curettage were examined histologically; one of these showed adenocarcinoma, though there was no evidence of this at subsequent hysterectomy. The post-operative sequelae were those ordinarily encountered after repair operations; wound healing was reported as good. The follow-up period varied from 1 to 20 years and the results on the whole were good, an analysis showing that a dosage of 1,200 mg.-hours was adequate. No patient subsequently developed carcinoma of the body of the uterus, though one developed carcinoma of the ovary and another a carcinoma of the colon.

This study reveals no contraindication to the proposed technique, but until such time as the work of Corscaden is confirmed, and the questions are settled of the alleged carcinogenic effect of intracavitary radium and the predisposition of women with late menopause to develop corpus carcinoma, such a technique should be used with discretion. *Ruth Dearing*

See also Section Endocrine Disorders, Abstract 1622.

RADIODIAGNOSIS

1447. **Roentgen Diagnosis of Lipoma of the Corpus Callosum**
W. H. Mullen and J. R. Hannan. *Radiology* [*Radiology*] **55**, 508–516, Oct., 1950. 5 figs., 17 refs.

The tissue of a lipoma is more translucent to *x* rays than normal cerebral tissues. A lipoma of the corpus callosum therefore appears on the radiograph as a well-outlined, radiotranslucent area, particularly in the lateral view. The periphery of such a lipoma is frequently calcified, but the amount of calcification varies considerably; it may be hardly perceptible or, in extreme cases, may have a bony density. In the sagittal view the calcification usually appears as two fairly dense, curvilinear deposits surrounding the centrally situated area of decreased density. There are no radiographic signs of increased intracranial pressure.

Air encephalography, which is not essential for diagnosis, shows a dilatation of the lateral ventricles and increased separation of the parts of the ventricles adjacent to the tumour. The medial borders of the lateral ventricles adjacent to the tumour are concave. The variations in the encephalogram depend on whether or not there is also agenesis of the corpus callosum. If the tumour is small and flattened from side to side encephalography may show only insignificant ventricular changes. *A. Orley*

1448. **Biophysical Studies of Methods utilizing Fluorescein and its Derivatives to Diagnose Brain Tumors**
G. E. Moore, D. A. Kohl, J. F. Marvin, J. C. Wang, and C. M. Caudill. *Radiology* [*Radiology*] **55**, 344–356, Sept., 1950. 4 figs., 13 refs.

The technique used by the authors for the diagnosis and location of brain tumours with fluorescein is briefly as follows. All patients who are to be subjected to craniotomy receive, immediately before operation, an injection of 1 g. of sodium fluorescein. At the operation the suspect areas of the brain are examined under ultra-violet light, fluorescence of the suspect area in cases of superficial tumour, or of tissue fragments from deeper-lying tumours, being indicative of the presence of abnormal tissue. In a series of 104 cases of suspected tumour only 8 tumours were found which showed no fluorescence, while of the 7 cases in which no tumour was found, fluorescence of the brain tissue was found in one only.

Attempts to render brain tumours radio-opaque by means of fluorescein compounds containing iodine or heavy metals were unsuccessful.

However, the selective retention by brain tumours of radioactive diiodofluorescein has proved useful for

diagnosis and location, although tumours of certain types or of small size do not retain a sufficient amount of the dye to make their detection practicable with the Geiger–Müller counter. The possibilities for improving this technique, and the development of the scintillation counter, are briefly outlined. Most of the dye is excreted in the bile except in cases of biliary obstruction, when it is excreted in the urine. There is little danger of ^{131}I splitting off from the dye and being taken up by the thyroid. *A. Orley*

1449. **Angiocardiopneumography in the Diagnosis of Pulmonary Tumours.** (L'angiocardiopneumografia nella clinica dei tumori del polmone)
M. Battezzati, F. Soave, A. Tagliaferro, N. Macarini, L. Oliva, and A. Piazza. *Minerva Medica* [*Minerva med., Torino*] **2**, 633–643, Oct. 6, 1950. 55 figs., 10 refs.

In this paper, based on the investigation of a series of cases of pulmonary neoplasm at the Radiological Institute of the University of Genoa, the authors outline the history of angiocardiography and describe the application of this method to the investigation of intrathoracic neoplasms in order to facilitate the work of the surgeon and enable a more precise diagnosis to be made before operation.

Their technique is based on that of Robb and Steinberg (*Amer. J. Roentgenol.*, 1939, **41**, 1 and 1941, **46**, 646). Under local analgesia an antecubital vein is isolated, preferably the cephalic or one of its tributaries. As large a cannula as possible is introduced into the vein and 20 to 30 ml. of normal saline run through. The contrast medium, in 70% concentration, is injected as rapidly as possible, not more than 3 seconds being required for 70 ml. They advocate the sitting position because they consider that gravity assists the flow of contrast medium. [In the abstracter's experience, angiocardiography is more satisfactorily performed with the patient lying; the flow of contrast medium may be assisted by positioning the arm.] Four exposures are made, about 7 seconds being taken for the injection and exposures. The procedure is usually well tolerated by the patient, there being merely a sense of discomfort and heat passing off in a few minutes, but attention is drawn to two possible causes of death: (1) delayed, from primary renal disturbance, and (2) immediate, from anaphylaxis due to abnormal sensitivity to contrast medium.

The authors claim that by means of angiocardiography it is possible to show the relation of a tumour to the heart and great blood vessels, whether the superior vena cava is directly invaded by the tumour or whether its lumen is compressed, and also whether the tumour is diffuse. When the superior vena cava is only displaced a localized tumour or cyst is probable. Innocent neoplasms insinuate themselves between vessels and usually cause little compression, even when large. With malignant bronchial tumours of infiltrating type there is partial or complete occlusion of main vessels and branches in the affected area; the branches of the pulmonary artery become displaced, deformed, or entirely occluded by neoplasms of the hilar region. Malignant tumours of small or medium bronchi at least modify the vascular pattern, but in the case of peripheral tumours this may only be shown on the lateral view. The degree of vascularization and retention of contrast medium in the affected area helps to indicate the nature of a tumour, but non-opacification of medium or small vessels does not always indicate malignancy. Chronic inflammatory processes will modify the normal vascular pattern. In mediastinal and extrapulmonary tumours the vascular pattern is essentially normal, although there may be some deviation of a whole segment. Apart from surgery, angiocardiography may be the only means of differentiating some aneurysms from mediastinal neoplasm. *Sydney J. Hinds*

1450. **Angiocardiography in Artificial Pneumothorax**
I. Steinberg, H. I. McCoy, and C. T. Dotter. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 353–359, Oct., 1950. 6 figs., 21 refs.

The angiocardiographic findings in the pulmonary circulation of living patients with artificial pneumothorax are illustrated. Angiocardiography usually demonstrates avascularity at the site of moderately, or far, advanced lesions of pulmonary tuberculosis.

After artificial pneumothorax the following changes may be noted: (*a*) decrease in the vascularity of the collapsed lung in proportion to the degree of collapse; (*b*) delay in rate of the blood flow in the collapsed lung; (*c*) crowding, distortion, and displacement of the pulmonary blood vessels in the collapsed lung; (*d*) varying degrees of shift of the heart, great vessels, and mediastinum to the side opposite the pneumothorax.

In " fibrothorax " following re-expansion of pneumothorax, angiocardiography serves to delineate the cardiovascular structures. Retraction and torsion of the cardiovascular structures and decreased vascularity to the affected side are demonstrated.

These angiocardiographic findings serve to supplement and confirm previous studies made on post-mortem material. Changes shown by the latter method are apparently not due to agonal processes but represent the vascular status during life.—[Authors' summary.]

1451. **Mediastinal Emphysema**
J. A. Evans and T. R. Smalldon. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 375–390, Sept., 1950. 12 figs., 37 refs.

This paper presents a discussion of the mechanisms of production of mediastinal emphysema, the significance of this disorder in the various clinical situations in which it occurs, and roentgen features of typical examples selected from a series of 50 cases collected at The New York Hospital.

Emphasis is placed on the importance of perialveolar and perivascular extension as demonstrated by Macklin and Macklin in evaluating dyspnoea and cyanosis in cases of acute pulmonary infection, in asthmatics, in the newborn, and in postoperative cases where trauma to pleura or extension of air from operative site to mediastinum seems unlikely. Postero-anterior roentgenograms may demonstrate one or both mediastinal pleural reflections or may reveal a globular radiolucency super-

imposed on the cardiac shadow. It is the lateral projection, however, which in the majority of cases is the most revealing in outlining mediastinal collections of air.

After operation, trauma to the chest, and in cases of spontaneous chest pain, dyspnoea and cyanosis should arouse suspicion of the presence of mediastinal emphysema. These signs and symptoms following operative procedures are usually considered to be due to the shock of the operation, some pulmonary complication, or sequelae of the anesthesia, and it is only when subcutaneous emphysema appears that the real nature of the condition is considered. Early recognition is therefore imperative if prompt corrective measures are to be instituted.

Several other points are made: (1) The relationship of pneumomediastinum to pneumothorax and subcutaneous emphysema; (2) the value of roentgen examination of the chest before tracheotomy to rule out mediastinal emphysema as the cause of extreme dyspnoea and cyanosis; and (3) the importance of early roentgen diagnosis in order to prevent the development of so-called " malignant " pneumomediastinum which may be fatal.—[Authors' summary.]

1452. **Radiographic Changes in the Lungs during Recovery from Drowning**
J. J. ROMAGOSA, L. J. MENVILLE, and J. T. LECKERT. *Radiology* [*Radiology*] **55**, 517–521, Oct., 1950. 2 figs., 8 refs.

The authors give a brief report of the radiographic and clinical findings in a patient who recovered after submersion in water for an unknown length of time. The abnormal radiographic changes in the lungs are believed to be primarily due to pulmonary oedema.

A. Orley

1453. **A Comparison of Bronchographic Techniques. (" Lipiodol " and " Ioduron ").** (Techniques comparées de bronchographie. (Lipiodol—ioduron))
A. BARANGER and P. DELIE. *Annales d'Oto-Laryngologie* [*Ann. Oto-laryng.*] **67**, 585–593, Aug.–Sept., 1950. 7 refs.

The authors compare the advantages and disadvantages of the iodized oils hitherto generally used for bronchography with those of a new product, " ioduron ", a viscous diiodide preparation soluble in water, the use of which requires the adoption of a different bronchographic technique. Briefly the procedure used by the authors for bronchography with the oily preparation is as follows: (1) Preliminary bronchoscopy is always carried out. (2) Morphine and atropine are given and amethocaine is used to anaesthetize the sub-glottic region, trachea, and bronchi. (3) A soft rubber catheter is introduced towards the desired side and about 1 ml. of amethocaine is again introduced. " Lipiodol " at room temperature is then injected; being only slightly viscous it spreads rapidly in a thin layer, and the radiographs can be taken at once. Ioduron has the consistency of a liquid jelly. Preparation of the patient takes longer than when oil is used, as the surface anaesthesia must be deeper and more extensive since ioduron is inclined to give rise to coughing and a massive dose is given. The medium is injected through a catheter in the usual way and its progress can be watched on the *x*-ray screen as it is injected.

The advantages of using the oily medium are that it is fluid and produces no irritation and that the radiographs can be taken at once. The chief disadvantage is its slow rate of elimination from the lung, making subsequent radiographs difficult to interpret. Conversely, the main advantage of ioduron is its rapid elimination, the lung fields being clear one hour after its use. In addition, owing to its viscosity, radiographs can be taken at the exact moment when fluoroscopy shows the affected area to have been reached. Its chief disadvantage, as previously observed, is that it promotes coughing and requires a more careful and prolonged preparation of the bronchial passages. It is therefore considered preferable to use an oily medium for bronchography in children and dyspnoeic subjects.

E. D. Dalziel Dickson

1454. **The Technique of Bronchography with a New Water-soluble Contrast Medium, " Ioduron 'B' "** (Technique de la bronchographie au ioduron " B ", nouveau produit de contraste hydrosoluble)
V. PARCHET. *Annales d'Oto-Laryngologie* [*Ann. Oto-laryng.*] **67**, 594–602, Aug.–Sept., 1950. 15 refs.

Hitherto the use of iodized oil for bronchography has been almost universal. Apart from the risk of producing iodism by its injection in large doses, the chief disadvantage of such an oily medium is its slow elimination, often prolonged into months and years, reducing the available respiratory surface and making subsequent radiographic examination of the lung fields difficult, if not impossible. With the introduction of a new contrast medium, " ioduron B ", a diiodide which is soluble in water and rapidly eliminated, these disadvantages would appear to have been eliminated. It is viscous, stable, and non-toxic, and is eliminated from the lung fields in about 20 to 30 minutes after injection. It is thus possible with ioduron to carry out serial bronchography, and there is the further advantage that any operative procedure such as lobectomy or pneumonectomy indicated on bronchography can be undertaken without delay. It is also possible to incorporate prophylactic doses of antibiotics such as streptomycin or penicillin in the medium when necessary.

The chief disadvantage of ioduron as compared with iodized oil is that it is more irritant, and its use necessitates more careful and extensive local anaesthesia, it being essential to anaesthetize not only the respiratory passages, but also the different lobes and segments which require to be explored. The author gives a detailed account of the technique of preparation; amethocaine, 1 or 2% with the addition of 20% naphazoline (" privine ") is used after premedication with pentobarbitone. In expert hands the whole undertaking takes about 30 to 40 minutes when one lung is to be examined, but although the procedure is longer and somewhat more complicated than that normally used, it does not present any great difficulty and the disadvantages are overwhelmingly outweighed by the advantages of using the water-soluble medium.

E. D. Dalziel Dickson

1455. **Roentgen Examination in Mesenteric Thrombosis**
J. FRIMANN-DAHL. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 610–616, Oct., 1950. 9 figs., 3 refs.

A short survey is given of the clinical features and radiological findings in 17 cases of mesenteric thrombosis at Ulleval Hospital, Oslo. While it may occur anywhere in the mesenteric circulation, this condition usually affects the portion of the superior mesenteric artery supplying the caecum and adjacent portions of the ascending colon and lower ileum. It is usually associated with local arteriosclerotic disease and is therefore rare in patients under 40. The onset is usually marked by severe pain, often persistent. Vomiting and the presence of blood in the stools are important clinical findings. Unless treated, the affected segment of bowel becomes gangrenous, while even with surgery the outlook is poor, only 3 of the 17 patients under review having recovered. Although the condition is seldom diagnosed before operation, *x*-ray examination, while not always conclusive, is often helpful in its early recognition. Plain films show multiple gas-filled loops of small intestine with fluid levels. If the colon is involved, as is usually the case, the affected part will be distended with gas and may show fluid levels. A barium meal will show retention of contrast medium in the affected loop without gross distension, together with thickening and rigidity of the mucosal pattern due to oedema.

The condition must be differentiated from acute regional enteritis and mechanical obstruction. The former condition usually occurs in the upper jejunum, but if the lower ileum is affected distinction may be impossible. In mechanical obstruction distention is usually more marked and the gas-filled loops appear hoop-shaped and the fluid levels longer than in thrombosis. In the early stages serial films should be taken—in thrombosis there may be a rapid increase in the number and size of the gas-filled loops within a few hours; this does not occur in mechanical obstruction. In doubtful cases a barium-meal examination may exclude occlusion of the small intestine, while a barium enema would eliminate colonic obstruction. The possibility of demonstrating the vascular occlusion directly by means of aortography or mesenteric angiography is mentioned. *J. A. Shiers*

1456. **Phlebography of the Pelvic Vessels.** (Ulteriore contributo alla conoscenza della flebografia dei vasi pelvici)
G. CICCARELLI. *Urologia* [*Urologia, Treviso*] **17**, 377–383, Oct. 20, 1950. 6 figs., 2 refs.

The author describes a technique of phlebography of the pelvic veins as an aid in the diagnosis of prostatic carcinoma [though whether this method would ever be widely adopted is very doubtful]. It consists in introducing contrast medium into the deep dorsal vein of the penis for the purpose of radiographic visualization of the prostatic plexus. It is essential that after the medium has been introduced sodium citrate in physiological saline be run in constantly until the examination is completed, as otherwise thrombosis will result: for the same reason the catheter used should be lightly lubricated and the medium used non-irritating. The prostatic plexus thus outlined shows itself as a complicated network of vessels the individual outlines of which it is not possible to distinguish. In the lateral view there can usually be made out four groups of vessels (two on each side) which drain this plexus. The author has studied 6 cases of prostatic carcinoma by this method and states that the radiological appearances were considerably modified in that the network of vessels was greatly reduced, if not absent altogether. This change, according to the author, is due to sclerosis of the periprostatic tissues from the neoplasm. [The diagnosis of carcinoma in the cases examined was a clinical one.] *S. M. Vassallo*

1457. **Radiographic Studies of Duodenum and Jejunum in Man**
J. W. MCLAREN, G. M. ARDRAN, and J. SUTCLIFFE. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.*] **2**, 148–164, Oct., 1950. 13 figs., 9 refs.

In these cinematograph studies direct films 5 inches (12·6 cm.) square were used. There were two exposures per second for a period of 20 seconds and the total amount of radiation [? skin dose] was of the order of 10 r. Each film was copied eight times on to 16-mm. film so that on projection at 16 frames per second each serial film was projected for half a second and the true intestinal speed was reproduced. The slight discontinuity of movement is considered an advantage as it emphasizes slight movements which might otherwise pass unnoticed.

" Conclusions reached in this work have been derived from a study of over 30 volunteers, involving over 100 examinations." An extensive questionary was completed to exclude subjects with any digestive or other abnormality. The examination was carried out in the morning, and the individual was requested to fast from the previous night. [It is not stated whether aperients were recommended or prohibited.] The meal consisted of 4 oz. (113 g.) of barium sulphate mixed to a cream with normal saline. The subjects were screened prone on a specially devised stretcher which ensured uniform conditions of pressure. When the barium reached the required site, an area was chosen as free as possible from obscuring coils and bony structures. The stretcher and subject were then rapidly and accurately positioned over the serial radiographic equipment. During exposure the subject held his breath in a neutral position after slight over-ventilation.

The following types of movement were noted: (1) Non-progressive segmentation which lasts about 4 seconds. (2) Progressive segmentation; the time taken to move on a mass of barium is about 3·5 to 6 seconds, and the distance travelled is of the order of 10 cm. (3) Rush peristalsis; only a few examples of this were recorded, but the rate of travel is stated to be approximately 60 cm. in 12 seconds. (4) Ring contractions or partial ring contractions (incisurae) appeared in 4 seconds, persisted for 4 seconds, and disappeared in 4 seconds. (5) Intrinsic mucosal pattern change: " In the second part of the duodenum the mucosa has been observed to change from a ' pavement ' type to a feathery type in

about ½ second, stay in the feathery formation for 2 seconds, and return to a pavement type in ½ second."

[Little attention seems to have been paid to controls. When similar work was carried out in Germany in 1935 the subjects were put through dummy runs (without being exposed to radiation) day after day for a fortnight before the actual test was made. Unless elaborate precautions are taken excitable states are common.]

Denys Jennings

1458. **The Tannic Acid Barium Enema in Colonic Investigation**

R. A. KEMP HARPER and J. H. L. CONWAY-HUGHES. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.*] **2**, 168–176, Oct., 1950. 20 figs., 24 refs.

The addition of tannic acid to a barium enema helps to demonstrate the mucosal pattern in three ways: tannic acid makes the suspension viscid and helps it to adhere to the mucosa; its astringent action inhibits the secretion of mucus, which tends to prevent barium adhering; after tannic acid the whole colon tends to contract and hence there is a more satisfactory emptying pattern. Two tablets of cascara are given 2 nights before the examination, and if this does not produce satisfactory results the dose is repeated. On the morning of the examination a thorough colonic wash-out is performed. The opaque enema is freshly prepared for each session. To a 2½% solution of tannic acid (200 gr. (13 g.) to the pint (0·5 litre)) 8 oz. (248 g.) of barium sulphate is added. A suspending agent such as tragacanth cannot be used as this prevents deposition of the barium. The enema container is suspended 4 ft. (1·2 m.) above the patient; a soft rubber catheter is used for children and young adults and a metal introducer with a rounded nozzle for older patients. In elderly patients where the musculature is poor or where there is a lack of co-operation a rubber catheter with an inflatable balloon is employed; the authors find that this nearly always prevents reflux. A few films are reproduced [but the scale is too small to show detail adequately].

Denys Jennings

1459. **Double-contrast Studies of the Colon with Special Reference to Preparation and Fictitious Polyps**

C. W. YATES, R. D. MORETON, and E. M. COOPER. *Radiology* [*Radiology*] **55**, 539–544, Oct., 1950. 6 figs., 3 refs.

In the course of double-contrast barium-enema examinations shadows resembling those cast by polypi are frequently observed. In such cases the examination has to be repeated in order to distinguish between the constant shadows of polypi and transient shadows caused by faecal matter, mineral or vegetable oil globules, water-insoluble grease from the enema cannula or proctoscope, and air-bubbles. These transient shadows are less frequently observed when the patient is allowed to have a small breakfast before the examination. However, when the primary object of the examination is to study the caecum, breakfast should be omitted to avoid excitation of the gastro-colic reflex.

In preparation for double-contrast examination, the best laxative is castor oil, while the most suitable enema solution is that prepared from castile soap-suds; no grease should be used to lubricate the cannula. Briefly, the routine suggested is: no supper on the night before; 1 oz. (28·4 ml.) of castor oil at 6 p.m.; beginning at 6 a.m., three small enemata at 15-minute intervals; a small breakfast at 7 a.m.; and the *x*-ray examination carried out at 8 a.m.

A. Orley

1460. **Roentgen Diagnosis of Tuberculous Salpingitis.** [In English]

K. EKENGREN and Å. B. V. RYDÉN. *Acta Radiologica* [*Acta radiol., Stockh.*] **34**, 193–214, Sept., 1950. 38 figs., 25 refs.

After reviewing the limited literature on the use of salpingography in the diagnosis of tuberculous salpingitis, the authors discuss the findings obtained in 75 cases of this disorder confirmed by operation. In all these cases salpinography, employing a water-soluble viscous iodine preparation, was carried out: 95 control examinations were made on patients undergoing investigation for sterility and in whom subsequent operation showed no macroscopic or microscopic evidence of tuberculosis.

The authors divide the radiological appearances in the tuberculous cases into 7 types: (1) Slightly dilated, smooth, club-like tubes showing a block in the ampulla or isthmus. (2) Like the foregoing, but ragged in contour near the site of obstruction. (3) Showing multiple strictures in the ampullary or isthmus region. (4) Moderately dilated tubes showing mucosal relief in the ampulla. (5) Dilated tubes with regular longitudinal mucosal ridges. (6) Like (5), but showing irregular hypertrophy of the mucosa in the ampulla. (7) Slightly or moderately dilated tubes with irregular filling defects and a ragged contour. Of the control subjects, the greatest number (53) showed dilated smooth-walled tubes not found in any of the tuberculous cases: in 17 the findings resembled those of type (4) of the tuberculous series, and in 16 the findings resembled those of type (5). These two types, therefore, cannot be regarded as diagnostic of a tuberculous condition. The other types had very few representatives among the control cases.

In 27 cases the condition was studied over long periods and the course of the disease followed on radiographs. The majority showed development of multiple strictures. Where the picture remained unchanged the greatest number of cases were those of type (1). In no case was there any evidence of the spread of the tuberculous process as a result of the salpingography. The procedure is considered a very valuable aid to the diagnosis of the tuberculous salpinx, a water-soluble medium having advantages over an oily medium.

A. M. Rackow

1461. **The Value of Roentgen Examination in the Diagnosis of Bronchogenic Cancer**

P. F. MØLLER. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.*] **2**, 102–117, Oct., 1950. 24 figs.

See also Section Respiratory Disorders, Abstract 1600; and Section Infectious Diseases, Abstract 1728.

Pathology

EXPERIMENTAL PATHOLOGY

1462. **Mitotic Activity in the Parathyroid Glands of the Rat following Bilateral Nephrectomy**
H. PLATT. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 383–387, Oct., 1950. 6 refs.

Mitotic activity was studied in serial sections of whole parathyroid glands from three series of rats: normal animals, those in which laparotomy and visceral manipulation had been carried out, and animals subjected to bilateral abdominal nephrectomy. Animals were killed 18 to 80 hours after operation. Up to 48 hours after nephrectomy there was no significant difference in the mitotic indices (number of mitoses per 100,000 cells). Glands examined at 60 hours or later showed an increased mitotic rate. It is suggested that this increased activity represents a final stage in the adaption of the parathyroids to an increased level of functional activity.
W. S. Killpack

1463. **Co-operative Effects of Endocrinological Factors and Processes of Ageing in producing Adenoma-like Structures in Rats**
V. KORENCHEVSKY and S. K. PARIS. *Cancer* [*Cancer*] **3**, 903–922, Sept., 1950. 40 figs., 29 refs.

1464 (*a*). **Studies on the Experimental Epidemiology of Respiratory Infections. I. An Apparatus for the Quantitative Study of Air-borne Respiratory Pathogens**
W. R. LEIF and A. P. KRUEGER. *Journal of Infectious Diseases* [*J. infect. Dis.*] **87**, 103–116, Sept.–Oct., 1950. 10 figs., 19 refs.

An elaborate apparatus is described for the exposure of animals to measured doses of air-borne bacteria, consisting of a chamber equipped with an atomizer and a sampling apparatus, and with special arrangements for the introduction of more animals without having first to sterilize the chamber. The apparatus was fitted with a number of instruments and devices to ensure safety for the operator.
Scott Thomson

1464 (*b*). **Studies on the Experimental Epidemiology of Respiratory Infections. II. Observations on the Behaviour of Aerosols of *Streptococcus zooepidemicus***
I. L. SHECHMEISTER and L. J. GOLDBERG. *Journal of Infectious Diseases* [*J. infect. Dis.*] **87**, 117–127, Sept.–Oct., 1950. 3 figs., 14 refs.

Before exposing animals to infection in the atmosphere of the chamber described in the first article (see Abstract 1464 (*a*)) elaborate examinations were made of aerosols of *Streptococcus zooepidemicus*, including estimation of the number of cocci in chains before and after atomizing, the measurement of the diameter of particles released from the atomizer, and the variation in the bacterial content of the mists in relation to distance from the nozzle of the atomizer.
Scott Thomson

1464 (*c*). **Studies on the Experimental Epidemiology of Respiratory Infections. III. Certain Aspects of the Behavior of Type A Influenza Virus as an Air-borne Cloud**
I. L. SHECHMEISTER. *Journal of Infectious Disease* [*J. infect. Dis.*] **87**, 128–132, Sept.–Oct., 1950. 25 refs.

Studies somewhat similar to those previously reported (see Abstract 1464 (*b*)) were made with influenza-A virus in aerosols. It was established that the virus was more infectious to animals when introduced by the air-borne route than by intranasal instillation.
Scott Thomson

1464 (*d*). **Studies on the Experimental Epidemiology of Respiratory Infections. IV. A Particle Size Analyzer Applied to the Measurement of Viable Air-borne Bacteria**
L. J. GOLDBERG. *Journal of Infectious Diseases* [*J. infect. Dis.*] **87**, 133–141, Sept.–Oct., 1950. 7 figs., 5 refs.

The physical factors influencing the particle size of aerosols were elaborately studied and a method of determining the sizes of bacteria-containing particles was obtained. The conclusions applied particularly to conditions where the range of sizes was not too great.
Scott Thomson

1465. **Effect of High and Low Oxygen Levels and Intermittent Positive Pressure Breathing on Oxygen Transport in the Lungs in Pulmonary Fibrosis and Emphysema**
H. L. MOTLEY and J. F. TOMASHEFSKI. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 189–196, Oct., 1950. 1 fig., 9 refs.

The elevated alveolar–arterial oxygen gradients of hard-coal miners with silicosis and other respiratory conditions were studied, and the effects determined of breathing 11·5 to 27·8% oxygen in nitrogen, and of intermittent positive-pressure breathing with compressed air. The difference in the oxygen partial pressures of the inspired air and alveoli was termed the aeration gradient; that between the arterial blood and alveoli, the transfer gradient.

The authors found that patients breathing a low level of oxygen showed a decreased transfer gradient, whereas at high levels it was increased. With low mixtures the aeration gradient decreased, but with mixtures richer in oxygen it increased. Intermittent positive-pressure breathing produced a decrease in both aeration and transfer gradients and a marked increase in arterial oxygen. It is suggested that intermittent positive-pressure breathing increased the arterial oxygen saturation by inflating alveoli the ventilation of which was otherwise impaired, thus producing more uniform alveolar aeration. The increased alveolar–arterial oxygen gradients in these cases is therefore attributed to inadequate alveolar aeration rather than to increased resistance to diffusion in the pulmonary membrane.
D. H. Sproull

1466. **Myocardial Infarction Induced Experimentally by Subadventitial Irritation of the Aorta.** (Infarctus myocardique expérimental par irritation sous-adventitielle de l'aorte)
R. LAPLANE and J. PAUTRAT. *Archives des Maladies du Cœur et des Vaisseaux* [*Arch. Mal. Cœur*] **43**, 888–902, Oct., 1950. 7 figs., 8 refs.

In experiments on 32 rabbits and 51 dogs under general anaesthesia, with artificial respiration maintained by tracheal intubation, the ascending aorta was exposed and 0·03 to 0·05 ml. of an irritant was injected into the subadventitial layer at several adjacent points. Of the various irritants tried, the best was croton oil diluted 1 in 400 or 1 in 500 with cholesterinated oil and then sterilized. Rabbits proved to be unsuitable subjects, while of the 36 dogs satisfactorily injected, 10 died within 1 to 2 days of a generalized haemorrhagic inflammation, although the procedure seems to have caused little initial shock or pain.

Electrocardiographic (ECG) records were taken, with standard bipolar leads, before and usually 4 days, 7 days, and 1 month after operation, further tracings being taken if the animal was not killed. A full series of records was obtained from 20 animals, which are classified in three groups: (1) tracings showed isolated changes (13 animals); (2) tracings showed changes in QRS and ST suggesting anterior myocardial infarction (6 animals); (3) changes in cardiac rhythm (2 animals).

Histological examination was carried out on 2 rabbits and 11 dogs. There were 3 types of lesion: (1) Vasomotor disturbances with oedema, vasodilatation, and diapedesis of erythrocytes. (2) Lesions of smaller vessels with oedema and venous thrombosis. (3) Degeneration of muscular fibres amounting in places to necrosis. In 7 animals correlation of ECG and morbid anatomical findings was possible and satisfactory. In those animals with the second type of ECG tracing, both histological and electrocardiographic results were exactly similar to those produced by ligation of the coronary artery.

The authors maintain that the underlying mechanism producing these lesions is a spasm of the arterioles and point out that all grades of lesion have been produced, including transitory ECG lesions without permanent histological changes. This fact, they feel, might explain those cases of myocardial infarction in man where no thrombosis and little or no atheroma is found.

Peter Harvey

1467. **The Importance of Methionine and Choline in the Arrest of Dietary Cirrhosis of the Liver in the Rat**
E. R. JAFFÉ, R. W. WISSLER, and E. P. BENDITT. *American Journal of Pathology* [*Amer. J. Path.*] **26**, 951–967, Sept., 1950. 6 figs., 30 refs.

Rats were fed on a low-protein, high-fat diet known to produce early fibrotic changes in the liver in 70 days, and well-marked cirrhosis in 111 days. After 70 days the protein (casein) was changed for an amino-acid mixture (supplemented by various known amounts of methionine and choline), and the animals were examined after a further 30 days. In this way it was possible to assess the effects of these substances quantitatively. About 60 mg. of methionine or about 30 mg. of choline a day caused cirrhosis to be very slight or absent. This effect is associated with the ability to cause disappearance of the large type of fat droplet seen in the liver cells.

Cystine interfered with the ability of these substances to prevent cirrhosis, but high levels of cystine did not increase hepatic fibrosis. *D. M. Pryce*

1468. **The Effect of Alloxan Diabetes on Experimental Cholesterol Atherosclerosis in the Rabbit. III. The Mechanism of the Inhibition of Experimental Cholesterol Atherosclerosis in Alloxan-diabetic Rabbits**
G. L. DUFF and T. P. B. PAYNE. *Journal of Experimental Medicine* [*J. exp. Med.*] **92**, 299–317, Oct. 1, 1950. 4 figs. 31 refs.

A study of the serum lipids in normal and alloxan-diabetic rabbits during the course of cholesterol feeding is presented, particular attention being paid to the factors considered to be responsible for the stability of the serum lipids; namely, (1) their interrelations and (2) their association with the serum proteins.

As far as the interrelations of the lipids were concerned a definite correlation was found between the development of atherosclerosis and an increase of serum cholesterol that was out of all proportion to the increase of serum lipid phosphorus and neutral fat. When these last two lipid constituents rose almost parallel with the serum cholesterol (as they did in some alloxan-diabetic rabbits), then the development of atherosclerosis was inhibited. This correlation was independent of the diabetic state, *per se*. It appeared likely that the marked elevation of serum neutral fat and lipid phosphorus in the diabetic animals was due to mobilization of body fat because of the disturbed carbohydrate metabolism. Because of their hydrophilic and emulsifying properties it was thought probable that the elevation of the phospholipids was the important factor responsible for the stability of serum cholesterol. That neutral fat played a role, however, could not be denied.

In normal rabbit sera, as we have previously shown, only small proportions of the lipid phosphorus and cholesterol are "readily extractable" (*i.e.*, unattached or only loosely attached to protein). On the other hand, in every case in which the serum lipids were elevated, the greater proportion of the lipid phosphorus and cholesterol was "readily extractable", irrespective of whether atherosclerosis developed or was inhibited. Analysis of the lipid content of the aorta of rabbits not fed cholesterol, whether diabetic or non-diabetic, and from alloxan-diabetic rabbits fed cholesterol but protected from the development of atherosclerosis, showed that there was no significant difference in lipid content or composition among the animals of these groups. When atherosclerosis developed following cholesterol feeding the lipid composition of the aortas was essentially the same in both control and diabetic animals. The deposited lipid consisted predominantly of cholesterol with small and fairly constant proportions of other lipids that did not vary significantly regardless of the quantities of these other lipids present in the circulating blood.

In the less severe lesions the proportion of ester cholesterol was greater than that of free cholesterol, but in advanced lesions the reverse was true.

The following conclusions are drawn concerning the pathogenesis of experimental cholesterol atherosclerosis in the rabbit: (1) Instability of cholesterol in the blood rather than hypercholesterolemia, *per se*, is the general condition responsible for the deposition of this substance in the arterial walls. (2) Of the factors considered to be responsible for the stability of the lipids in the blood, the interrelations of the lipids appear to be more important than their relation to the serum proteins, at least in so far as the development of experimental cholesterol atherosclerosis is concerned. The importance of these conclusions in relation to the pathogenesis of human atherosclerosis is discussed.—[Authors' summary.]

1469. **The Effect of a Deficiency of the B Vitamin Complex (except Thiamine) on the Blood Pressure of the Rat**
P. MERRITT. *Journal of Experimental Medicine* [*J. exp. Med.*] **92**, 333–336, Oct. 1, 1950. 4 figs., 4 refs.

On feeding rats on a diet deficient in the vitamin-B complex (except aneurin), Calder (*J. exp. Med.*, 1942, **76**, 1) observed a persistent rise in blood pressure, and by using a partially deficient diet induced pathological changes in the kidneys. The author fed four groups of rats, 25 in each group, on diets similar to those used by Calder, but with the addition of choline chloride in two of the groups to eliminate the possible effect of lipotropin deficiency. The rise in blood pressure reported by Calder was not observed, nor were the pathological renal changes found except for some degree of tubular atrophy. On the other hand, intracellular granules of haemosiderin were found in the renal tubules. This effect is undergoing further investigation. *R. B. T. Baldwin*

1470. **An Example of Hormonal Antagonism in the Pathogenesis of Disease; Oestradiol and Progesterone and Necrosis of the Uterine Mucosa due to Diphtheria Toxin.** (Ein Beispiel von Hormonantagonismus bei der Krankheitsentstehung. Östradiol–Progesteron und Nekrose der Uterusmukosa durch Diphtherietoxin)
E. TONUTTI and K. H. MATZNER. *Neue Medizinische Welt* [*Neue med. Welt*] **1**, 1361–1366, Oct. 21, 1950. 1 fig., 17 refs.

In five series of experiments with guinea-pigs it was shown that the administration of oestradiol facilitated the production of haemorrhagic necrosis of the uterine mucosa by the intracardiac injection of 5 to 10 MLD of diphtheria toxin, whereas progesterone suppressed this necrosis. Oestradiol and progesterone exercised a mutually antagonistic effect in relation to the reaction of the vascular tissue of the uterus to diphtheria toxin. This is regarded by the authors as one more example of the dependence of tissue reaction to a severe bacterial intoxication upon hormonal influences, and they suggest that in suitable cases of diphtheria in women high therapeutic doses of progesterone should be given in order to diminish the toxic effect on the uterus. They also suggest that it might be of importance to give similar doses in other severe infections, particularly during pregnancy. *Norval Taylor*

1471. **Experimental Pyelonephritis in the Rabbit produced by Staphylococcal Infection**
S. DE NAVASQUEZ. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 429–436, July, 1950. 10 figs., 5 refs.

Non-pathogenic bacteria were detected in rabbits' kidneys (removed at operation and incubated for 18 hours) only up to 2½ hours after intravenous injection. These organisms were never isolated from the urine, this indicating non-penetration of epithelial barriers. The pathogenic organism used was *Staphylococcus aureus* Oxford strain, and a number of initial experiments were necessary to determine a suitable dose to ensure that the rabbits survived a sufficient time for suppurative pyelonephritis to develop. The dose arrived at was 50 million organisms per ml. per kg. body weight. Of 6 rabbits 3 died in 5 to 6 days with suppurative pyelonephritis and the others were killed after 2 or 3 months. After initial pyuria lasting 3 days with a heavy growth of *Staph. aureus* on culture there was no further urinary abnormality.

Histologically, in the early stages serial sections showed a number of disconnected foci of suppuration affecting the whole length of a nephron. A typical focus had three zones: a central bacterial colony, intermediate coagulative necrosis, and peripheral polymorphonuclear infiltration. The healed lesions were roughly triangular, depressed scars very similar to those ascribed to atherosclerosis in man. In one surviving rabbit a chronic perinephric abscess was found, and another showed diffuse amyloidosis with mucoid metaplasia of the pelvic and collecting-tubule epithelium. *W. S. Killpack*

1472. **Observations on the Behaviour of the Transplanted Kidney in Dogs**
W. J. DEMPSTER. *Annals of the Royal College of Surgeons of England* [*Ann. R. Coll. Surg. Engl.*] **7**, 275–302, Oct., 1950. 18 figs., 46 refs.

A third kidney transplanted into a dog ceased to produce urine on the fifth day. Along with the anuria the temperature and blood pressure rose sharply and the dog became anorexic and vomited. Removal of the homotransplanted kidney brought dramatic improvement, the temperature and blood pressure becoming normal in 12 hours. This result was similar to that of other authors, except that the " toxic syndrome " had not been previously noted. The transplanted kidney was oedematous and necrotic; the interstitial tissue was heavily infiltrated with polymorphonuclear leucocytes, lymphocytes, and plasma cells. The author concludes that similar homotransplantation of the kidney in humans would be dangerous and useless.

A study was made of the activity of the transplanted kidney, the dog being its own donor. The technique of transplantation into the neck, the circulation being interposed between the carotid and jugular, is fully described. Urinary flow from the autotransplanted kidney occurred usually within 15 minutes of opening up the new circulation. Observations were made on 50

dogs in which the transplanted kidney excreted for periods ranging from 3 days to 8 weeks (two only): many failures are reported and an analysis is given of the causes of failure, such as massive necrosis or disengagement of the renal artery. In successful cases urine was collected by a soft plastic indwelling catheter passed well up the ureter. Observations were made in unilaterally nephrectomized animals on the behaviour of the kidney before and after transplantation. After transplantation a persistent polyuria developed associated with an inability to concentrate urine (hyposthenuria). Albumin was present only during the first 48 hours. Pyelography revealed normal dye excretion. Renal blood and glomerular flow in the transplants varied from 50 to 90% of that in the abdominal kidney.

The auto-transplanted kidney responded adequately by diuresis to a given load of water in a hydrated animal. When the auto-transplant was made to compete with an existing normal kidney under similar circumstances it did not respond as efficiently when the dosage of water was repeated. Inhibition of water-diuresis by "emotional stress induced by faradic stimulation" occurred alike in the transplant and abdominal kidney. Intravenous injection of "infundin" had the same effect. The author considers this supports Verney's theory that water diuresis is effected by a posterior pituitary hormone. Electrolytes were handled less efficiently by the transplant than by the normal kidney. The former allowed greater sodium loss and inefficient retention of sodium and chloride in salt depleted animals. The possible factors responsible for the polyuria and hyposthenuria are discussed but no conclusion is reached.

[The original paper should be read by those interested.] *B. G. Maegraith*

1473. **The Dynamics of Parenchymatous Embolism in Relation to the Dissemination of Malignant Tumours**
J. S. Young and H. D. Griffith. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 293–311, July, 1950. 25 figs., 18 refs.

All living animal tissues, neoplastic as well as non-neoplastic, contain a system of vascular tubes invested by a semi-solid medium, the pressure of which may differ from that of the fluid inside the tubes. A hydrostatic model was constructed, embodying this principle and consisting of a tank filled with fluid traversed by a collapsible tube, in order that a study might be made of the factors governing the ingress and egress of fluids containing suspended bodies through holes in the wall of the tube. The tank was filled with a mixture of 1 part glycerine and 4 parts water in which polystyrene beads were suspended, the same fluid without the beads being circulated through the tube. It was found that when the pressure within the tube fell, due to a decreased rate of internal flow, the suspended bodies readily passed through the holes from without. The conclusion is drawn that embolus formation from normal tissue possessing no penetrative ability is determined by a change in differential pressure between the tissues and the vessels, such as occurs notably with trauma. Similar experiments in which N/5 sodium hydroxide was passed through the tube, which was immersed in glycerol jelly at *p*H 6 containing phenolphthalein, were also performed.

The frequent occurrence of focal haemorrhages in malignant tumours and the findings with the hydrostatic model suggest that the embolic spread of tumour cells may well be determined by simple hydrostatic means and not necessarily by virtue of their invasive growth properties. Though little is known of the pressures in small lymphatics it seems reasonable to assume that tumour cells may gain access to them in the same way. The physical principles governing the flow of fluids through non-rigid tubes are outlined in an appendix to the paper. *W. S. Killpack*

1474. **The Significance of the "Tissue Pressure" of Normal Testicular and of Neoplastic (Brown–Pearce Carcinoma) Tissue in the Rabbit**
J. S. Young, C. E. Lumsden, and A. L. Stalker. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 313–333, July, 1950. 16 figs., 14 refs.

The Brown–Pearce carcinoma was propagated through 60 generations in rabbits (5 to 20 at a time). Tumour cells were implanted in one testis only in each animal. By a specially-designed manometric method the tissue pressure was estimated in the developing tumour at various stages, and simultaneously in the healthy contralateral testis. Results in individual tumour-bearing testes showed a wide scatter, but the pattern of readings in the intact organ was sufficiently constant to show that the method of measurement was a reliable one; although technical hitches were frequent, due allowance was made for these.

It was found that the tissue pressure of the tumour was constantly substantially greater than that of the normal testis, and that it increased with the lapse of time until widespread necrosis supervened, preventing the taking of readings. The tissue pressure of the normal testis remained stationary; in both normal and neoplastic tissues the extravascular pressure was raised by injections of small amounts of fluid and by digital compression. These observations suggest that common clinical procedures in tumour diagnosis in man may well be factors in the dissemination of tumour material.
W. S. Killpack

1475 (*a*). **Damage Induced in Sarcoma 37 with Podophyllin, Podophyllotoxin, *alpha*-Peltatin, *beta*-Peltatin, and Quercetin**
J. Leiter, V. Downing, J. L. Hartwell, and M. J. Shear. *Journal of the National Cancer Institute* [*J. nat. Cancer Inst.*] **10**, 1273–1293, June, 1950. 8 figs., 31 refs.

The effect of injection of various substances present in podophyllin resin on grafts of sarcoma 37 was tested. Minced tumour tissue was injected intramuscularly into genetically homogeneous hybrid mice, and the test substance injected subcutaneously 6 days later, remote from the tumour. It was found that 3 substances present in crude podophyllin, podophyllotoxin, α-peltatoxin, and β-peltatoxin, produced cellular damage followed by gross haemorrhage and necrosis in the grafts, while a fourth, quercetin, was much less active. Cellular damage was

detectable after 2 hours, and gross changes after 6 hours. The 3 active components accounted for most of the activity of the crude podophyllin; all 3 had about the same minimum effective dose (M.E.D.) (2 μg. per g. body weight) and maximum tolerated dose (M.T.D.) (30 to 40 μg. per g. body weight). The crude drug was equally toxic, but one-fifth as effective. Intravenous and subcutaneous routes were about equally effective, but by the oral route the M.E.D. was 10 times greater, and the M.E.D./M.T.D. ratio was increased.

M. H. Salaman

1475 (*b*). **Effect of *alpha*-Peltatin, *beta*-Peltatin, and Podophyllotoxin on Lymphomas and other Transplanted Tumours**

E. M. GREENSPAN, J. LEITER, and M. J. SHEAR. *Journal of the National Cancer Institute* [*J. nat. Cancer Inst.*] **10**, 1295–1333, June, 1950. 33 refs.

The effect of these components of podophyllin on the growth of 5 grafted tumours was tested, the technique being as described above (Abstract 1475 (*a*)). An acute stem-cell leukaemia, a metastasizing and a local lymphosarcoma, a mammary adenocarcinoma, and a melanoma, transplanted in various pure-line or hybrid mice, and a "carcino-sarcoma" in rats, were used. After a single injection of any of the 3 substances, cellular changes followed by gross damage were observed in all the tumours in varying degree, metastases responding in the same way as primary growths. For the leukaemia and the lymphosarcomata the minimal single effective dose was the same as for sarcoma 37 (see Abstract 1475 (*a*)). It was higher for the carcinoma, and highest for the melanoma. The maximum tolerated dose varied according to the size of the tumour and whether or not it had been previously treated. In melanoma-bearing mice it was markedly lowered. Repeated injections retarded tumour growth in all cases, but never resulted in complete regression. Shrinkage of spleen and thymus was produced in both normal and leukaemic mice, and the rise in the number of stem-cells in the blood of the latter was delayed. Loss of body weight, or failure to put on weight, was associated with the effect on the tumour, but a similar reduction of body weight by starvation had no comparable effect on the tumour.

M. H. Salaman

1476. **Beryllium and Growth. 1. Beryllium-induced Osteogenic Sarcomata**

M. B. HOAGLAND, R. S. GRIER, and M. B. HOOD. *Cancer Research* [*Cancer Res.*] **10**, 629–635, Oct., 1950. 10 figs., 6 refs.

Twenty-four rabbits received intravenous injections at 6- or 4-day intervals of saline suspensions of finely-ground insoluble compounds of beryllium. Seven rabbits developed osteogenic sarcomata after 11 to 24 months; 8 died within 3 months. The primary tumours were situated in the femur in 4 rabbits and in the humerus, tibia, and ischium each in 1 rabbit. Secondary growths were present in 5 of the rabbits. The tumours were highly invasive; the shaft of bone at the site of origin was sometimes completely destroyed. Histologically the growths consisted of osteogenic sarcomata varying from extreme anaplasia to well-differentiated bone-forming tissue. The secondary tumours were usually less well-differentiated than the primary. The duration of the disease from the first symptoms or *x*-ray signs until death was 1 to 2 months. Conspicuous fibrosis of the liver was present in rabbits that developed sarcoma as well as in those that did not. The serum alkaline-phosphatase activity rose rapidly in rabbits that developed sarcoma in parallel with the dissemination of the tumour, and the activity of the enzyme in the tumour tissue itself was extremely high. The phosphatase, like normal alkaline phosphatase, was activated by magnesium and inhibited by beryllium. It is suggested that the inhibitory action of beryllium on phosphatase activity may be an important factor in its tumour-inducing power.

L. Foulds

MORBID ANATOMY

1477. **A Histologic Study of Muscles and Nerves in Poliomyelitis**

J. DENST and K. T. NEUBUERGER. *American Journal of Pathology* [*Amer. J. Path.*] **26**, 863–881, Sept., 1950. 16 figs., 16 refs.

In the early stages of poliomyelitis the muscles showed an irregularity in staining associated with a granular fatty degeneration of many fibres. Longitudinal fibrillation and sometimes necrosis were seen. Later many fibres showed atrophic shrinkage (? disease atrophy) and some hypertrophy. Proliferation of sarcolemmal nuclei and formation of muscle giant cells were sometimes conspicuous, but definite evidence of regeneration was absent. In all stages the histological appearances were characteristically pleomorphic. Changes in the nerves (which were obvious by the third day) were less severe than those in muscle, but it seemed that the degree of damage in the muscles and anterior horn cells ran parallel. The muscle changes, however, differed from those of simple central paralysis, and may possibly be due to a direct action of the virus. *D. M. Pryce*

1478. **Toxic Lesions of the Pancreas**

P. V. VÉGHELYI, T. T. KEMÉNY, J. POZSONYI, and J. SÓS. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 390–403, Sept., 1950. 6 figs., 10 refs.

The authors believe that scarlet fever and certain other acute febrile illnesses of childhood are commonly complicated by toxic degeneration of the pancreas, with diminished enzyme secretion. The lesions are readily reversible.

The present paper describes pancreatic changes induced in white rats by administration of bacterial toxins or, more regularly, carbon tetrachloride. The pancreas proved to be more susceptible than the liver to these poisons. The pancreatic changes varied from vacuolation of parenchymal cells in the mildest cases to complete degeneration of all secreting tissue except the islets of Langerhans, which were unaffected. The pancreas was shown to have remarkable powers of regeneration and of

recovery from these lesions. Cystic degeneration of the pancreas was common. It was thought to be acinar, not obstructive, in origin. The picture closely resembled that of human cystic fibrosis of the pancreas and, like it, might be associated with cystic dilatation of bronchi.

Martin Hynes

1479. **Pathologic Lesions in Cystic Fibrosis of the Pancreas**

W. L. BOSTICK and J. F. RINEHART. *Journal of Pediatrics* [*J. Pediat.*] **37**, 469–477, Oct., 1950. 14 refs.

Details of 20 cases of cystic fibrosis of the pancreas in patients ranging in age from 20 days to 12 years are given in tabular form with particular reference to the pathological findings. These cases were encountered in a series of 363 necropsies performed during a 26-year period at the University of California Hospital. They constituted a quarter of the cases classified as of coeliac disease. Although full examination of all tissues was not performed as a routine measure, especially in the earlier cases, the duodenum showed cystic dilatation of Brunner's glands in 10 out of the 12 cases examined. The pathological findings in the pancreas and the lungs which are now so well known are described in some detail and the authors emphasize that they could find no correlation between the degree of pancreatic destruction and the severity of the coeliac syndrome. *David Morris*

1480. **Hemolytic Disease of the Newborn Infant (Erythroblastosis Fetalis). A Study of the Pathologic Lesions of Twenty Cases**

S. LINDSAY. *Journal of Pediatrics* [*J. Pediat.*] **37**, 582–598, Oct., 1950. 19 figs., 6 refs.

The author describes the pathological findings in 20 children with haemolytic disease of the newborn who were examined in the Division of Pathology, University of California School of Medicine. Microscopical observations were controlled by similar examinations on 60 children who had not suffered from the disease.

Of the children with erythroblastosis, 15 had been jaundiced, oedematous, or both, while 4 had been oedematous only and 5 had been neither jaundiced nor oedematous. The heart was above the average weight in 11 cases, but showed no abnormality microscopically. The liver was from 15 to 240 g. above the average weight in 12 cases, and showed abnormal centres of haematopoiesis diffusely distributed throughout the liver, but mainly in the sinusoids. This was equally marked in oedematous cases and in jaundiced cases, and led to marked distortion and degeneration of the liver cells. The degree of liver damage varied with the amount of haematopoietic activity. The reticulo-endothelial cells contained pigment granules. In the majority of cases the spleen was enlarged. Lymphoid follicles were small, and in some cases absent, and there was diffuse haematopoiesis throughout the splenic pulp in all cases. The adrenal glands in most cases were heavier than normal, the cortical layers appearing thickened. Microscopically, the majority of cells of the follicular and reticular layers were vacuolated, and there were areas of necrosis and calcification. The thyroid gland in 19 cases appeared hyperplastic, with small follicles lined with tall columnar cells and containing no colloid. The pancreas in many cases showed an increase in the size and number of islets. The kidneys in 12 cases were heavier than average; there was considerable degeneration of the convoluted tubules and pigment casts were found in the convoluted and collecting tubules. There was some haematopoietic tissue, mainly interstitial.

In 15 cases the only abnormality in the brain was evidence of oedema. In 5 it was bile-stained; the more pigmented the brain, the more damaged it appeared to be, the basal and medullary nuclei being most affected. The neurons showed signs of degeneration and in some cases calcification had occurred. In diffusely stained brains pigment granules could be found between the swollen glial cells. The affected nuclei showed vascular congestion, but in no case was vascular thrombosis found. The bone marrow was more cellular than usual, with a decrease in the granular cells and an irregularity of cell pattern. The intestine showed submucosal haematopoiesis throughout its length with replacement of the lymphoid follicles by haematopoietic tissue in some areas. *H. G. Farquhar*

1481. **The Histogenesis of Granular-cell Myoblastoma (? Granular-cell Perineural Fibroblastoma)**

A. G. E. PEARSE. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 351–362, July, 1950. 16 figs., 34 refs.

A histological and histochemical examination of 6 specimens of granular-cell " myoblastoma " is described, and the three hypotheses concerning the origin of these lesions—whether from muscle cells, histiocytes, or Schwann cells—are rejected. The granules in the cells are found to stain similarly to granules in fibroblasts. It is suggested that the growths are lipoid-containing granular-cell fibroblastomata. *R. A. Willis*

1482. **Cytological Changes in Human Hypophyses after Cortisone and ACTH Treatment**

G. L. LAQUEUR. *Science* [*Science*] **112**, 429–430, Oct. 13, 1950. 2 refs.

CLINICAL PATHOLOGY

1483. **The Sedimentation Differential Agglutination Test. I. Method of the Test. II. Observations on the Destruction and Production of Red Blood Cells, with Special Reference to Myeloblastic Leukemia and Comparison with the Results of the Radioactive Phosphorus Method**

D. STATS. *Blood* [*Blood*] **5**, 950–963, Oct., 1950. 6 figs., 7 refs.

The period of time during which transfused erythrocytes remain in the circulation of a recipient is usually determined by means of the indirect differential agglutination test of Ashby in which group-O erythrocytes are transfused into a recipient of another group. At suitable intervals potent anti-serum is used to agglutinate the recipient's own cells in a sample of blood, and the

unagglutinated cells belonging to group O are counted. The author uses a similar method, but instead of counting the unagglutinated cells, the relative volume of the agglutinated cells after settling for a period of time in a sedimentation tube is measured. The method relies upon the fact that erythrocytes washed free of plasma with physiological salt solution and resuspended therein settle very slowly because agglutination does not take place. If the cells are of different groups and an agglutinating serum affecting one of these is added, the affected cells will settle rapidly and leave the others behind in suspension. The agglutinating serum used has to be calibrated with standard mixtures of erythrocytes to determine the relationship between the volume of agglutinated sediment and the number of agglutinable cells.

Simultaneous measurements by this "sedimentation differential agglutination" method and by means of radioactive phosphorus were made; good correspondence between the results by the two methods was observed.

In the course of these studies the author noticed in several patients suffering from myeloblastic leukaemia that there was a two-fold cause of anaemia. There was a complete—or almost complete—lack of formation of erythrocytes or delivery to the circulating blood and, in addition, active haemolysis. According to the author, it is the latter which, in patients suffering from "blast anaemia", frequently prevents the attainment of optimum levels of erythrocytes by blood transfusion, except for very short periods of time. *H. Lehmann*

1484. **Intravital Staining of Cutaneous Carcinoma with Triphenyl Tetrazolium Chloride. Its Possible Clinical Applications**

O. CANIZARES and P. MICHAELIDES. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 157–159, Sept., 1950. 1 ref.

Tetrazolium salts are water-soluble and colourless, and solutions in contact with certain reductases in living tissues are reduced to insoluble red compounds known as formazans. This reaction has been seen to develop *in vitro* with freshly removed carcinomatous tissue. An attempt was made to apply this reaction to the diagnosis of cutaneous carcinoma. Studies were also made of ulcers, burns, gummata, and warts. Results were not sufficiently constant to be of practical value.

James Marshall

1485. **The Excretion Kinetics of the Dye T-1824 in Relation to Plasma Volume Determinations**

A. E. LEWIS and R. D. GOODMAN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 599–603, Oct., 1950. 1 fig., 5 refs.

1486. **The One-stage Prothrombin Consumption Test. Clinical Value in the Identification of Thromboplastin-deficiency Diseases**

M. STEFANINI and W. H. CROSBY. *Blood* [*Blood*] **5**, 964–972, Oct., 1950. 3 figs., 13 refs.

The formation of a solid clot does not represent the end-point of the intricate complex of reactions leading to the coagulation of blood or plasma. In haemophilia, acquired haemophilia-like diseases, and severe thrombocytopenia there is always impaired activation by thromboplastin. In the presence of a minimal amount of thromboplastin enough thrombin may, however, be formed eventually to clot fibrinogen, but much residual prothrombin will be found in the serum. The purpose of the prothrombin consumption test is to identify this residual prothrombin activity. The test requires deprothrombinized plasma, thromboplastin, and a standard curve of plasma prothrombin activity. This curve is prepared by determining the prothrombin time of serial dilutions of deprothrombinized with normal plasma. Each mixture is assumed to possess a percentage of normal prothrombin activity corresponding to the percentage of normal plasma it contains, and the correlation of prothrombin time with this figure results in an exponential curve. Reference to this curve allows the conversion of other prothrombin time values into percentages of normal prothrombin activity. For the test, the serum from 2 ml. of clotted blood is mixed with $\frac{1}{10}$ volume of sodium citrate and incubated for 30 minutes to allow the neutralization of thrombin. The clotting time is then recorded after adding, in rapid succession to a test tube kept at 37° C., 0·1 ml. of each of the following: (1) deprothrombinized plasma; (2) 0·02 M calcium chloride; (3) thromboplastin; and (4) the serum to be tested.

The serum prothrombin activity was below 10% in 11 normal subjects. In 2 cases of thrombocytopenic purpura the values were 87% and 63% respectively; 24 hours after splenectomy they had fallen to 6% and 0·8% respectively. Out of 7 cases of thrombocytopenia due to leukaemia in only one was the value below 10% (9·8%); in one it was 15%, in 2 between 30% and 40%, and in the remaining 3 above 60%. Similar results were obtained in one case of aplastic anaemia (34%) and 2 cases of haemophilia (68% and 91%); in 2 cases of pseudohaemophilia, 5 cases of hypothrombinaemia due to dicoumarol treatment, and 3 cases of polycythemia vera the values obtained were all below 10%.

The authors have examined the effect on the validity of the test of the presence of different amounts of serum accelerator and conclude that it is unaffected. Though normal serum has a high accelerator content, there is little prothrombin to act upon. Even 100% acceleration of prothrombin activity is of no practical significance when the residual level is only 2%. On the other hand, in a serum where there has been little prothrombin consumption, accelerator content is negligible.

H. Lehmann

1487. **Experimental Investigations on Local Changes in the White Blood Cell Picture following Perforating Injury to Blood Vessels (Veins)**

W. GRAF and Å. SWENSSON. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 419–427, July, 1950. 3 figs., 20 refs.

The lateral marginal vein of the ear of a rabbit (which had been starved for 24 hours) was punctured by a medium-sized needle which was then rotated within the lumen to produce endothelial injury. The authors

report a local intravascular accumulation of leucocytes, with an increased proportion of basophils in comparison with that found in the systemic circulation, in the first drop of blood taken from the site of repeated puncture of the same vein at 30-minute intervals over a period of 2½ hours. The total leucocyte count in blood obtained after continued "milking" from the site of puncture was lower than that in the first drop. Films stained in 1% toluidin blue in 60% alcohol for 20 minutes followed by 1% toluidin blue in water for 20 seconds demonstrated the basophilic granules more clearly than May–Grünewald–Giemsa preparations. *Ernest T. Ruston*

1488. **Simplified Procedure for Determining the Renal Clearance of Inulin and Diodone**
O. OLBRICH, M. H. FERGUSON, J. S. ROBSON, and C. P. STEWART. *Lancet* [*Lancet*] **2**, 565–567, Nov. 18, 1950. 3 figs., 9 refs.

1489. **The Nature of the Renal Circulatory Changes in Chronic Congestive Failure as Reflected by Renal Tubular Maximal Functions**
J. CROSSMAN, R. E. WESTON, J. P. HALPERIN, and L. LEITER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1320–1326, Oct., 1950. 2 figs., 31 refs.

To determine whether the renal circulatory changes in chronic congestive heart failure affects all nephrons proportionately, the following investigations were performed on 15 young patients (5 male, 10 female) with rheumatic carditis: (1) glomerular filtration rate (G.F.R.); (2) renal plasma flow (R.P.F.); (3) maximal tubular capacity for excreting *para*-aminohippurate (Tm_{PAH}), a measure of functional tubular excretory mass; and (4) maximum tubular capacity for reabsorbing glucose (Tm_G), a measure of the number of functioning intact nephrons.

The G.F.R. (mean=88·5 ml. per minute per 1·73 sq. m.; σ=14·0) was found to be reduced from 46·4 to 93·2% of corresponding average normal values for the respective sexes. The R.P.F. (mean=277 ml. per minute per 1·73 sq. m.; σ=74·0) was reduced even further, from 20·2 to 72% of the normal average values. The filtration fraction was thus increased from the normal average of 0·19 to 0·20 to a mean value of 0·34. The Tm_{PAH} was within normal limits in 12 of the 13 subjects in which it was estimated (mean=74·5 mg. per minute per 1·73 sq. m.; σ=14·6). The Tm_G was also within normal limits in all of 12 patients (mean=328 mg. per minute per 1·73 sq. m.; σ=70·8). There was no demonstrable relation between either the G.F.R. or R.P.F. and Tm_{PAH} on the one hand and the Tm_G on the other.

In conclusion, it is stated that the results of these experiments indicate that at least two tubular functions are not depressed in chronic congestive heart failure, in spite of renal ischaemia and hypoxia. There is in these cases a decrease in filtration in the glomerulus of each nephron, but no reduction in the tubular mass perfused. Thus, the possibility of any significant intrarenal "shunt" can be excluded. A final point discussed in this communication is the significance of the resulting glomerulotubular imbalance in relation to sodium and water retention in chronic congestive heart failure uncomplicated by hypertensive or arteriosclerotic renal disease.
A. I. Suchett-Kaye

1490. **The Use of Cation Exchange Indicator Compounds to Determine Gastric Acidity without Intubation**
H. L. SEGAL, L. L. MILLER, J. J. MORTON, and H. Y. YOUNG. *Gastroenterology* [*Gastroenterology*] **16**, 380–386, Oct., 1950. 1 fig., 3 refs.

Cation exchange resins suitable for use in the determination of gastric acidity should be linked to a radicle which is only displaced at a *p*H below 3·0—that is, by free acid—and must also be readily absorbed from the small intestine, excreted in the urine, and assayable by some simple method.

The batch of exchange resin used in these experiments was treated with quinine hydrochloride so that 1 g. of resin took up 20 mg. Tests *in vitro* being satisfactory, a test was made on 100 patients. Out of 63 patients with free acid in a 7% alcohol test meal, 59 excreted quinine in the urine in the first hour and 4 in the second. Of 27 patients with no free acid, none excreted quinine in the first hour, but 5 excreted small amounts in the second. This was ascribed to the very slight displacing effect of sodium, calcium, and potassium cations. The authors believe that this type of technique is capable of refinement and that it may well prove to give information as reliable as *p*H readings, since it dispenses with the abnormal stimulus of intubation. *Denys Jennings*

1491. **Intravenous Galactose Liver Function Test.** (Beitrag zur Leberdiagnostik unter Verwendung der intravenösen Galaktosezufuhr)
O. SCHILDKNECHT. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **80**, 219–224, March 4, 1950. 39 refs.

Thirteen healthy subjects and 7 patients with hepatic cirrhosis (the diagnosis being subsequently confirmed at necropsy) were given 60 ml. of 50% galactose intravenously over 5 minutes. Galactose disappeared from the blood in 30 and from the urine in 60 minutes in the healthy subjects. Urinary excretion was delayed in the cirrhotic patients, galactosaemia persisting for longer than normal. The oral galactose and cephalin tests gave positive results in only 4, and the Takata–Ara test in only 2, of the 7 cases. Application of the intravenous test to several other types of disease showed the test to be sensitive and reliable. *N. Policzer*

1492. **Use of the Step-photometer for Bilirubin Tolerance Tests of Liver Function.** (Применение ступенчатого спектрофотометра для функциональной пробы печени с нагрузкой билирубином)
N. M. MUSULJAK and A. A. SHELAGUROV. Терапевтический Архив [*Terap. Arkh.*] **22**, No. 5, 50–52, Sept.–Oct., 1950.

1493. **The Van Den Bergh Reaction**
N. W. ELTON. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 901–914, Oct., 1950. 19 refs.

Microbiology

1494. **Studies on the Extracellular Cultivation of an Intracellular Parasite (Avian Malaria). 1. Development of the Organisms in Erythrocyte Extracts, and the Favoring Effect of Adenosinetriphosphate**
W. TRAGER. *Journal of Experimental Medicine* [*J. exp. Med.*] **92**, 349–366, Oct. 1, 1950. 16 figs., 23 refs.

The value of previous investigations on the physiology of malaria parasites was limited by the fact that they were made on organisms living within the erythrocytes of their hosts. A new approach to the study of the nutrition and behaviour of these parasites is described by the author, who succeeded in cultivating *Plasmodium lophurae* outside the erythrocytes. Blood from infected ducklings was suspended in a nutrient medium containing a concentrated extract of duck erythrocytes. In this solution the parasites were freed of the host-cells by haemolysis after treatment with an anti-duck-erythrocyte rabbit serum, to which guinea-pig serum was added for complement. Small amounts of the suspension, containing numerous free parasites, were added to Erlenmeyer flasks with the nutrient medium, which was gelled by the addition of agar, gelatin, or duck plasma. The flasks, which were placed in a rocker at 39° to 40° C., were ventilated with a mixture of air (95%) and carbon dioxide (5%), and a liquid phase of the medium was added and replaced by fresh medium at 12-hour intervals. Under these conditions the parasites survived for 2 days and developed extracellularly, producing schizonts. These segmented to merozoites, which gave rise to trophozoites. The growth of the parasites was favoured by the presence in the medium of yeast adenylic acid and cozymase, and further by addition of adenosinetriphosphate and sodium pyruvate. On the 3rd day of cultivation the parasites were still normal in appearance, but later many degenerated and very few remained normal on the 5th day. The condition of the parasites was determined on morphological criteria based on microscopical examination of samples. A description is given of the structure of *P. lophurae*, as seen in fresh preparations by phase microscopy and in stained films, which is illustrated by a number of photomicrographs.

The composition of the medium and of various methods used are described in great detail [for which the reader is referred to the original]. *C. A. Hoare*

1495. **An Experimental Study of *Entamoeba muris* (Grassi, 1879); its Morphology, Affinities and Host–parasite Relationship**
R. A. NEAL. *Parasitology* [*Parasitology*] **40**, 343–365, Oct., 1950. 23 figs., bibliography.

Rats are now employed extensively as experimental hosts of *Entamoeba histolytica* in the screening of new chemical compounds for amoebicidal activity. One of the drawbacks in the use of these animals is the fact that both wild and white rats are commonly infected with an amoeba of their own (*E. muris*), the presence of which introduces a complicating factor in the experiments. On this account it is important to differentiate natural infections with *E. muris* from experimental infections with *E. histolytica*. In view of the discrepant accounts regarding the structure, bionomics, and systematic position of *E. muris*, the author has undertaken a revision of this parasite. In this paper he gives a detailed description of the morphology and development of the amoebae from rats and mice, from which he concludes that they are represented by one species, *E. muris*.

He then describes cross-infection experiments of rats, mice, and hamsters with their respective amoebae, which were found to be interchangeable. This fact accounts for the high incidence of infection with *E. muris* in laboratories where various rodents are kept together. In connexion with the above experiments the author also deals with the precautions which were successfully taken to prevent infection among the experimental animals under laboratory conditions. Since *E. muris* is indistinguishable from *E. coli* both in the active and encysted stages, in experiments carried out to determine the degree of host-restriction of the human parasite rats were used, as they are more likely to be contaminated with *E. coli* than mice. These animals were fed with cysts of *E. coli* from human faeces and from cultures, but the results were invariably negative. The entamoebae of rats and man thus differ in physiological characters. The author suggests that they be retained as distinct species until the metacystic development of *E. muris* is fully studied. He also discusses the incidence of similar entamoebae among other rodents, a list of which is provided.

[This paper should help to solve some of the difficulties in experimental amoebiasis of rodents which have baffled previous workers in this field.]

C. A. Hoare

1496. **A Study of the Pox Viruses by Complement Fixation and Inhibition of Complement-fixation Methods**
A. W. DOWNIE and A. MACDONALD. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **62**, 389–401, July, 1950. 2 figs., 16 refs.

In direct complement-fixation tests with mammalian sera there was little evidence of serological differences between the viruses of variola, alastrim, vaccinia, cowpox, and ectromelia, but by means of immune fowl sera and the technique of complement-fixation inhibition of Rice (*J. Immunol.*, 1948, **59**, 365; **60**, 11) it was possible to detect greater degrees of difference. In this test the highest dilution of immune fowl serum which would prevent the fixation of complement by a known fixing combination of mammalian serum and antigen, as found in preliminary tests, is determined. By this technique it would appear that four different strains of

variola (isolated at different times between 1944 and 1947 in different parts of the world) and the one alastrim strain were indistinguishable and very closely related to the two strains of vaccinia virus. But the two cowpox strains (isolated in 1937 and 1947) could be clearly distinguished from those of the variola–vaccinia group and were more closely related to that of ectromelia.

R. Hare

1497 (*a*). **Antibiotics and Lysis by Bacteriophage. VI. Action of Chloramphenicol on the Culture of a Staphylococcus and on the Lysis of this Culture by Bacteriophage.** (Antibiotiques et lyse bactériophagique. VI. Action de la chloromycétine sur la culture d'un staphylocoque et sur la lyse bacteriophagique de cette culture)

M. FAGUET and E. EDLINGER. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **79**, 472–475, Oct, 1950. 2 figs., 14 refs.

1497 (*b*). **Antibiotics and Lysis by Bacteriophage. VII. The Antiphage Action of Chloramphenicol.** (Antibiotiques et lyse bactériophagique. VII. L'action antiphage de la chloromycétine)

E. EDLINGER and M. FAGUET. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **79**, 436–442, Oct., 1950. 3 figs., 6 refs.

Chloramphenicol has only a very slight inhibitory action on the growth of *Staphylococcus albus*, but the rate of growth is slowed and after a considerable period a slow and progressive lysis of the organisms is seen. In moderate and high doses chloramphenicol inhibits lysis of staphylococci by bacteriophage: with very feeble doses lysis is retarded and interrupted; however, the phase in which turbidity of the culture is decreased by chloramphenicol is accelerated. *G. M. Findlay*

1498. **Studies on the Aetiology of Human Actinomycosis. I. The "Other Microbes" of Actinomycosis and their Importance.** [In English]

P. HOLM. *Acta Pathologica et Microbiologica Scandinavica* [*Acta path. microbiol. scand.*] **27**, 736–751, 1950. 48 refs.

Other organisms besides *Actinomyces bovis* have frequently been found in the lesions of actinomycosis, but no definite aetiological role has so far been attributed to them. The author investigated 960 specimens of material from cases of actinomycosis in Denmark between 1934 and 1949, paying particular attention to this aspect of the subject. The material was investigated by examination of smears, and by isolation in anaerobic culture of *Actinomyces* and accompanying organisms. Specimens had been taken from closed cavities or abscesses in approximately 650 instances; 360 of these were infections with *Actinomyces bovis*, but other types of *Actinomyces* were present in 290 cases and *Nocardia asteroides* in 2 cases. In all but one of the 650 cases (one of the cases in which *Nocardia* was present), the ray fungus was accompanied by some other type of organism. These included *Bacterium actinomycetem comitans*, an anaerobic Gram-negative bacillus of *Haemophilus* type, and other anaerobic Gram-negative coccobacilli and bacilli. These organisms tended to form definite associations with different types of *Actinomyces* in various situations. It is considered probable that the presence of these other bacteria is necessary for the production of disease, and that actinomycosis represents a mixed infection with *Actinomyces* and one or more commensal organisms.

D. J. Bauer

BACTERIA

1499. **An Acid-fast Microorganism Cultivated from Leprous Material. Bacteriological and Serological Observations**

M. TERNI. *International Journal of Leprosy* [*Int. J. Leprosy*] **18**, 161–167, April–June, 1950. 11 refs.

An acid-fast organism has been obtained in culture during the course of numerous attempts to isolate leprosy bacilli in the media of Dubos and Petragnani and in the larvae of *Galleria mellonella*. Material from a skin leproma was inoculated into six larvae, and 2 days later a transfer was made from one larva into tubes of medium. A single colony was obtained in a tube of Petragnani's medium after incubation for 3 months. In an investigation of the characteristics of the organism it was found to be acid-fast, Gram-positive, aerobic, and non-motile; it grew best at 37° C., and required glycerol. It was not pathogenic for laboratory animals. Antigens prepared from cultures of the organism reacted in complement-fixation tests with sera of leprous patients up to titres of 1 in 320. The organisms were not lysed by bacteriophages active against five species of mycobacteria, and it is concluded from a review of their properties that they were neither tubercle bacilli nor saprophytic contaminants. *D. J. Bauer*

1500. **Cytological Studies in Association with Local Injections of Streptokinase-streptodornase into Patients**

A. J. JOHNSON. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1376–1386, Oct., 1950. 5 figs., 28 refs.

An investigation has been made of the effects of injecting a mixture of streptococcal desoxyribose nuclease and streptokinase into empyemata and pleural effusions. In patients with non-purulent effusions [the number is not stated], the injection of the enzyme mixture caused an outpouring of polymorphonuclear leucocytes, and counts showed a more than ten-fold increase in cells within 24 hours. A second injection, given 3 to 5 days after the response had subsided, was followed by the appearance of even greater numbers of polymorphonuclear leucocytes. No response was produced by enzymes which had been inactivated by heat. Similar effects were noted in 11 patients with empyemata. From studies of motility and the examination of smears stained supravitally it was evident that the increase in the number of polymorphonuclear leucocytes was due to the appearance of new living cells and not to the release of degenerating cells from digested exudate. A marked increase also occurred in the phagocytic activity of the cells of the exudate. In patients who improved after the enzyme treatment polymorphonuclear leucocytes disappeared from the exudate and were replaced by

lymphocytes, and later by monocytes, macrophages, and endothelial cells. The injection of the enzymes had the additional effect of breaking up the clumps of polymorphonuclear cells, which was presumably brought about by the depolymerization of the desoxyribose nucleic acid contained in the exudate. This enzyme also depolymerized the nucleic acid of degenerating leucocytes so that they no longer stained by Feulgen's method, whereas viable leucocytes were unaffected; as a result of this, the percentage of degenerated cells observable in empyema fluids fell to a low value after the injection of enzyme. In conclusion it is pointed out that the enzyme treatment is of value for digesting cell debris, and replacing the degenerated leucocytes of a pleural exudate with living cells, with consequent beneficial effect.

D. J. Bauer

1501. **Antibiotics produced by Micrococci and Streptococci that Show Selective Inhibition within the Genus *Streptococcus***

R. G. E. Murray and L. J. Loeb. *Canadian Journal of Research, E. Medical Sciences* [*Canad. J. Res.* (E)) **28**, 177–185, Oct., 1950. 2 figs., 21 refs.

This paper comes from the Department of Bacteriology and Immunology, University of Western Ontario, Canada.

Five of 158 strains of *Micrococcus pyogenes* and two of 47 strains of *Micrococcus epidermidis* were found to produce antibiotics which inhibited the growth of a mucoid *Streptococcus pyogenes*. These antibiotics were also active against some Gram-positive organisms, but not against Gram-negative bacteria. On the basis of further experiments these 7 strains were divided into four groups producing antibiotics of different types.

Two of 3 strains of β-haemolytic streptococci which produced antibiotics were shown to inhibit all the mucoid and a few non-mucoid *Strep. pyogenes*. These observations suggest that apart from capsulation there may be a fundamental metabolic difference between the majority of mucoid and non-mucoid strains of *Strep. pyogenes*.

A. W. H. Foxell

1502. **Indican Excretion in Relation to Intestinal Sterilization**

W. E. Wooldridge, G. W. Mast, and M. Hoffman. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 501–510, Oct., 1950. 6 figs., 4 refs.

A combination of streptomycin with glucuronic acid has been shown, in work mostly unpublished, to reduce the number of bacteria in the large intestine. The authors used this combination to determine whether the elimination of indole-producing bacteria would be accompanied by a diminished urinary excretion of indican. Six patients were given 2 g. of streptomycin and 8 g. of glucuronolactone by mouth daily. The bacterial content of the stools was reduced to less than 1,000 organisms per g., but the urinary excretion of indican showed no appreciable change.

J. E. M. Whitehead

1503. **Determination of Streptomycin Resistance of *Mycobacterium tuberculosis* by Pryce's Technique.** (Determinacion de la estreptomicino-resistencia del mycobacterium tuberculoso con la tecnica de Pryce)

H. Bonfiglioli, A. Cetrángolo, and C. Acuña. *Prensa Medica Argentina* [*Prensa méd. argent.*] **37**, 2458–2461, Oct. 13, 1950. 2 figs., 14 refs.

The authors, working in the Institute Malbrán, have made a comparative study of the streptomycin-resistance of tubercle bacilli in 30 different sputa, using either Pryce's technique with a modified Dubos–Middlebrook medium (1·5 g. of phytone per ml. being added) or Herrold's medium. Results agreed in 18 cases, but in 3 cases greater resistance was found with Pryce's technique and in 6 cases with Herrold's medium: 3 cases were excluded owing to contamination or negative results.

Results were obtainable on the eighth day with Pryce's technique, but not until the twentieth day with Herrold's medium.

René Mendez

1504. **The Cytology of an Avian Strain of *Mycobacterium tuberculosis* Studied with the Electron and Light Microscopes**

G. Knaysi, J. Hillier, and C. Fabricant. *Journal of Bacteriology* [*J. Bact.*] **60**, 423–447, Oct., 1950. 25 figs., 32 refs.

The structure and microchemistry of the Sheard strain of *Mycobacterium tuberculosis* var. *avium* were studied with the electron and light microscopes. The transparency of the cytoplasm of this organism aided observations. Preparations were made by growing the organism on collodion films; organisms grown in submerged cultures were obscured by a densely opaque bacterial slime surrounding them. The cell consisted of a thin, highly ductile cell wall, a thin cytoplasmic membrane, a poorly staining cytoplasm containing many rod-shaped micellae of unknown nature, a few (up to 20) cell-sap vacuoles, and 1 to 5 nuclei. The cell-sap vacuoles contained material in solution and nearly spherical micellae. The resting nucleus consisted of a lipid-containing chromatin outer layer and a core which stained red with Giemsa's stain.

D. G. ff. Edward

1505. **Evaluation of the Coagulase Test in the Study of Staphylococci associated with Food Poisoning**

J. B. Evans, L. G. Buettner, and C. F. Niven. *Journal of Bacteriology* [*J. Bact.*] **60**, 481–484, Oct., 1950. 7 refs.

Tests for enterotoxin, carried out by introducing the supernatant fluid from cultures into the stomachs of rhesus monkeys, showed that 24 coagulase-negative strains of staphylococci isolated from food were non-enterotoxigenic. Most of the strains had been present in large numbers in food, and had been regarded as having caused outbreaks of food poisoning. Two coagulase-positive strains, isolated from the food in cases of food poisoning, were positive. Four out of 5 coagulase-positive strains originally isolated in small numbers from wholesome food, and 5 out of 7 coagulase-positive strains isolated from pyogenic staphylococcal infections, were also enterotoxigenic. A laboratory

accident, in which a spilled culture produced local furunculosis, showed that the same strain might be both pyogenic and enterotoxigenic. *D. G. ff. Edward*

1506. **Studies on Peroxidative Detoxification of Purified Diphtheria Toxin**
K. AGNER. *Journal of Experimental Medicine* [*J. exp. Med.*] **92**, 337–347, Oct. 1, 1950. 3 figs., 18 refs.

Diphtheria toxin, brought by fractional precipitation with ammonium sulphate and magnesium sulphate to a purity of 2,200 Lf per mg. N, was not detoxified by myeloperoxidase and hydrogen peroxide unless oxidizable dialysable cofactors were also present. Such cofactors are present in acid-hydrolysed casein and in human urine; uric acid is such a cofactor. The flocculation titre of toxin modified by treatment with myeloperoxidase, hydrogen peroxide, and cofactor remained unchanged even after 99% or more of the toxicity had been destroyed; small amounts of such partly detoxified toxin readily produced delayed paralysis in guinea-pigs.

In experiments in which mixtures of purified diphtheria toxin and myeloperoxidase were placed in a "cellophane" bag surrounded by hydrogen peroxide and casein hydrolysate, the fluid inside the bag took on an intense reddish-brown colour, which was not removable by dialysis of the contents of the bag against phosphate buffer. It is suggested that peroxidative detoxification of diphtheria toxin leads to the production of a coloured protein with the properties of a toxoid.

It is suggested that the spontaneous detoxification of diphtheria toxin with time is due to a slow peroxidative process. *C. L. Oakley*

1507. **Comparison of Seven Antibiotics against *Haemophilus pertussis* Infection in Chick Embryos**
G. G. JACKSON, M. W. BARNES, and M. FINLAND. *Journal of Immunology* [*J. Immunol.*] **65**, 419–424, Oct., 1950. 2 figs., 5 refs.

Fertile hen's eggs incubated for 7 days at 39° C. were used as the medium in comparative tests of the inhibition of *Haemophilus pertussis* by 7 different antibiotics—penicillin G, polymyxin B, streptomycin, aureomycin, neomycin, chloramphenicol, and terramycin. Into the yolk sac was injected 0·25 ml. of broth containing a suitable concentration of the antibiotic under test, followed immediately by 0·25 ml. of a dilution of *H. pertussis* culture containing 5×10^5 organisms (5×10^5 LD 50 per egg). All the antibiotics significantly prolonged life of infected embryos, a large proportion of them surviving for at least 10 days after infection. The effective prolongation of life and the percentage of survivors varied with the dose of antibiotic given; the relationships were different for each antibiotic tested. Moreover, with streptomycin and penicillin most deaths occurred early, whereas with polymyxin B and with the larger doses of chloramphenicol, deaths were infrequent until late in the period of observation. There appeared to be no relationship between antibiotic activity *in vitro* and *in vivo*. No antibiotic consistently sterilized infected eggs. *C. L. Oakley*

1508. **The Group Phase of *Shigella paradysenteriae* Type W: its Isolation from Man**
R. P. ELROD, K. OKABE, A. C. SANDERS, and R. L. HULLINGHORST. *Journal of Immunology* [*J. Immunol.*] **65**, 375–382, Oct., 1950. 11 refs.

IMMUNITY

1509. **The Separation of a Protective Antigen from a Toxin-producing Strain of *Hemophilus pertussis***
K. C. ROBBINS and L. PILLEMER. *Journal of Immunology* [*J. Immunol.*] **65**, 393–406, Oct., 1950. 1 fig., 29 refs.

Agglutination and agglutinin-absorption tests showed that *Haemophilus pertussis* strains 18 and 29 have a common antigen, while strain 18 has, in addition, an independent surface antigen. It was necessary to add 0·5% formalin to cultures of strain 29 to prevent disruption of the bacterial cells and thus preserve agglutinability. Of various fractions produced by treatment of the freeze-dried organisms of strains 18 and 29, those obtained by exposure to ultrasonics and to freezing and thawing gave the highest precipitin titres against sera from rabbits immunized with whole organisms adsorbed on aluminium cream or killed with phenol or thiomersolate. Water extraction, freezing and thawing in 0·15 M sodium acetate, and ultrasonic disruption in water at *p*H 7·2 gave the most active protective fractions, as judged by mouse-protection tests: extraction with water was chosen as the most simple method. The protective antigen can be partially separated from the heated, non-toxic, water extract by fractionation with methanol–water mixtures under controlled conditions of *p*H, ionic strength, and temperature. *C. L. Oakley*

1510. **The Antigenicity of *Shigella sonnei***
S. E. BRANHAM and S. A. CARLIN. *Journal of Immunology* [*J. Immunol.*] **65**, 407–417, Oct., 1950. 23 refs.

Female mice of a CFW strain weighing 12 to 14 g. were vaccinated, usually in groups of 100, with three intraperitoneal or subcutaneous injections of 0·5 ml. of a 5-hour broth culture (10^9 organisms per ml.) of a *Shigella* species treated with 0·4% formalin, at intervals of a week. One month after the last injection, groups of mice were challenged with varying numbers of test organisms suspended in mucin, the concentration of mucin used depending on the virulence of the test organism, and the "immunity index"—the ratio between the number of organisms killing 50% of the vaccinated animals and that number killing 50% of the controls—determined.

Vaccination with *S. shigae* 6, *S. paradysenteriae* III (Z), I (V), II (W), and *S. ambigua* gave low immunity indices (100 to 200,000) against the homologous strains; in contrast, vaccination with *S. sonnei* gave an immunity index of 10,000,000 against that organism. This marked antigenic capacity was limited to phase-I strains of *S. sonnei*; phase-II and phase-R strains gave an immunity index of only 10 to 2,000 against the homologous strains. Phase-I strains gave no protection against phase-II or

phase-R strains of *S. sonnei*, or against *S. ambigua*, *S. paradysenteriae* (VI) or *S. dysenteriae* 6 or 17, but gave slight protection against *S. paradysenteriae* II (W), I (V), and III (Z). Phase-II and phase-R strains of *S. sonnei* failed to protect against themselves, phase-I strains, or *S. paradysenteriae* to any great extent. Serum from rabbits immunized with *S. sonnei* phase I will, in very small amounts, protect mice against 1,000 fatal doses of *S. sonnei* phase-I; such sera give practically no protection against phase-II and phase-R strains. *C. L. Oakley*

1511. **The Alpha, Beta and Gamma Antigens of *Clostridium histolyticum* (Weinberg and Seguin, 1916)**
C. L. OAKLEY and G. H. WARRACK. *Journal of General Microbiology* [*J. gen. Microbiol.*] **4**, 365–373, Sept., 1950. 34 refs.

The authors investigated the culture-filtrates of a number of smooth strains of *Clostridium histolyticum* in order to identify the different types of antigenic component. They confirmed the presence of a lethal and necrotizing toxin, a collagenase, and a proteolytic enzyme which is cysteine-activated and attacks altered collagen, such as hide-powder, but not native collagen. These components are named α, β, and γ respectively. The two enyzmes attack gelatin. By carrying out a series of tests with sera from horses immunized with culture filtrates, in which culture-filtrate–serum mixtures and suitable indicators were used, it was found possible (by taking one particular serum as a standard) to assign numerical values to the antibodies to α, β, and γ antigens found in immune sera. *H. J. Bensted*

1512. **Serologic Studies of Mumps Employing Complement Fixation and Agglutination-inhibition**
A. E. FELLER and W. S. JORDAN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 360–368, Sept., 1950. 21 refs.

The authors have made a critical comparison of the agglutination-inhibition and complement-fixation tests in the serological diagnosis of mumps. The complement-fixing antigens were obtained from chick embryos infected with mumps virus, the virus-bound (V) antigen being obtained from allantoic fluid and the soluble (S) form from the chorio-allantoic membrane.

A four-fold or greater increase in complement-fixing titre against the V antigen was demonstrated in 13 of 14 pairs of acute and convalescent sera from cases of clinically established mumps. No such increase occurred in sera from 12 cases of "aseptic meningitis". Tests with the S antigen failed to confirm previous reports that this antigen detects antibody earlier than the V form; in 3 out of 11 cases the S antigen failed to detect a significant increase in titre, although a diagnostic increase had been found with the V antigen.

The agglutination-inhibition test revealed four-fold or greater increases in titre only in those sera showing a change of similar order against the V antigen. The complement-fixation test did not, however, appear to be superior to the agglutination test for diagnostic purposes, and both tests were of equal reliability.

In some cases the V antigen detected antibody in single sera from persons infected with mumps 20 to 30 years previously. The S antibody, however, fell to a low level within 1 to 2 years of infection. The agglutination-inhibition test was not a reliable index of past infection on single sera since all sera contained a heat-stable (56° C.) non-specific inhibitor. [Inactivation at 62° C. will usually differentiate between true mumps antibody and non-specific inhibitors.] *J. F. McCrea*

1513. **The Relationship of Complement-fixing and Anti-hemagglutinating Factors against the Viruses of Mumps and Newcastle Disease**
W. S. JORDAN and A. E. FELLER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 369–377, Sept., 1950. 17 refs.

Close antigenic relationship between the viruses of mumps and Newcastle disease of fowls has been shown in studies of their relative positions in the erythrocyte receptor-gradient, and also by the demonstration of a factor neutralizing Newcastle-disease virus in the sera of patients recently infected with mumps. In extending these observations the authors examined 71 pairs of acute and convalescent sera from patients hospitalized with infectious diseases, in which were included 15 cases of mumps.

A four-fold or greater increase in either complement-fixing or antihaemagglutinin titre against Newcastle-disease virus was found in 12 of the 15 cases of mumps; in 6 cases the titre had risen significantly in both tests, in 3 cases the complement-fixing, but not the antihaemagglutinin, titre increased, and in one case the reverse was true. In general, the relative increase in antibody against Newcastle disease ran closely parallel with the increase in specific antibody against mumps. The 56 pairs of sera from patients with diseases other than mumps were also tested for complement-fixation and antihaemagglutinins, but with one possible exception, where the complement-fixing titre rose, no significant changes were observed. Single sera from 96 "normal" individuals showed the neutralizing factor against Newcastle disease in 32 cases, and 90% of these sera also contained mumps antibody.

The results strongly suggest that the Newcastle-disease neutralizing factor is dependent on the presence of mumps antibody. Taken together with previous work on the close relationship of mumps and Newcastle-disease virus in the receptor-gradient, it is highly probable that the two viruses possess common antigenic components.
J. F. McCrea

1514. **The Effect of Injection of Diphtheria Prophylactic into Apparently Normal Horses**
M. BARR. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **31**, 615–625, Oct., 1950. 4 figs., 2 refs.

1515. **A New Method for the Large-scale Production of High-titre Botulinum Formol-toxoid Types C and D**
M. STERNE and L. M. WENTZEL. *Journal of Immunology* [*J. Immunol.*] **65**, 175–183, Aug., 1950. 1 fig., 22 refs.

Paediatrics

1516 (*a*). **The Haemoglobins of the Foetus and Newborn**
F. D. WHITE, G. E. DELORY, and L. G. ISRAELS. *Canadian Journal of Research, E. Medical Sciences* [*Canad. J. Res.* (E)] **28**, 231–237, Oct., 1950. 2 figs., 15 refs.

In addition to the so-called labile and refractory haemoglobins in the blood of the foetus and newborn infant, the authors report a third form which they have detected by following the rate of reaction with sodium hydroxide. They measured the haemoglobin concentration by observing optical densities in a spectrophotometer, and found three distinct breaks in the curves relating haemoglobin concentration and time. Two of the three reaction-rates correspond to the previously reported forms of haemoglobin, but the third rate was intermediate between these. This new component could be detected in only 33 of 66 samples of cord blood or blood from normal, full-term infants; its presence could not be correlated with any other factor and the authors could give no explanation of the anomaly.

Confirmation also was obtained of the presence of a labile and a refractory component of haemoglobin in adult blood; the evidence obtained from the rate of reaction with sodium hydroxide indicated that whereas the former fraction may be identical with the corresponding fraction in foetal blood, the refractory component of adult blood is not identical with either the newly reported or the refractory component of foetal blood.

R. P. Hullin

1516 (*b*). **The Role of the Foetal Haemoglobins in the Aetiology of Jaundice of the Newborn**
G. E. DELORY, L. G. ISRAELS, and F. D. WHITE. *Canadian Journal of Research, E. Medical Sciences* [*Canad. J. Res.* (E)] **28**, 238–244, Oct., 1950. 15 refs.

The total bilirubin, total haemoglobin, and refractory haemoglobin content of the blood was determined in a series of 32 normal, newborn infants at the Winnipeg General Hospital. The blood was obtained from the umbilical cord and by heel puncture at 1, 3, and 7 days, and again at 3 or 4 weeks, after birth. The total and refractory haemoglobin estimations were carried out as already described (see Abstract 1516 (*a*)), while the bilirubin was estimated by Waugh's method (*Amer. J. med. Sci.*, 1940, **199**, 9). Of the infants studied 19 developed clinical jaundice within the first 7 days of life; there was no threshold level of bilirubin at which all infants became jaundiced, but jaundice was present in all cases with plasma bilirubin greater than 4·5 mg. per 100 ml. The bilirubin level was at its highest by the 3rd day and had fallen by the 7th day in most of the cases, confirming the findings of previous workers. The total haemoglobin value rose sharply after birth, began to decline after the 3rd day, and reached the initial value in 3 to 4 weeks; these results are not in agreement with those of other workers.

The authors obtained a mean value of 76·2% (range 50 to 87%) of total for the refractory haemoglobin of cord blood; this mean value increased steadily up to the 7th day and then fell to the 3rd or 4th week, when there was evidence that the refractory component was decreasing faster than the other components of haemoglobin. This typical pattern was not followed in all the cases studied.

No correlation between the rate of destruction of total haemoglobin or of its refractory component and the degree of bilirubinaemia was noted. No evidence was found that the refractory haemoglobin fraction was more susceptible to destruction than the other fractions, nor did it appear to be selectively destroyed in the neonatal period; hence it would appear to be without special significance in the aetiology of neonatal jaundice.

R. P. Hullin

1517. **Factors Influencing Retention of Nitrogen and Calcium in Period of Growth. VIII. Influence of Rest and Activity**
J. A. JOHNSTON. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 551–565, Oct., 1950. 10 figs., 14 refs.

In this paper the author describes an attempt to determine the effect of moderate activity of the patient on the progress of healing (as indicated by nitrogen and calcium retention) in children with diseases normally treated with prolonged rest in bed. Previous clinical and animal experimental work on the harmful effects of inactivity on tuberculous, cardiac, and orthopaedic disorders is reviewed. Calcium balance tests over periods of 18 days were undertaken in 5 patients aged 7 to 15 suffering from tuberculosis and in 1 patient aged 13 with rheumatic carditis. These tests showed that calcium retention declined after the acute phase had passed, but that moderate activity (walking, or pedalling a " one-wheel bed bicycle ") led to calcium retention. The value of rest in the treatment of acute disease is generally accepted, but after the acute stage has passed prolonged inactivity is unwise. *R. M. Todd*

1518. **Absorption of Fat and Vitamin A in Premature Infants. II. Effect of Particle Size on the Absorption of these Substances**
S. MORALES, A. W. CHUNG, J. M. LEWIS, A. MESSINA, and L. E. HOLT. *Pediatrics* [*Pediatrics*] **6**, 644–649, Oct., 1950. 2 figs., 9 refs.

The effect of variation in particle size on fat and vitamin-A absorption was assessed in 6 healthy premature infants, aged 6 to 40 days. In each case observations were made during three experimental periods of 4 days each. During the first and third periods the diet consisted of butter fat (3% and 5% respectively) and fish-liver oil (5·3 ml. per l.) homogenized in skimmed milk. The fat globules after homogenization had a maximum

diameter of 2 μ. In the intermediate feeding period the diet was the same except that the fat and vitamin A were unemulsified. In all 6 infants fat absorption was much better when fat was finely emulsified, the average absorption of homogenized fat being 71·5% in contrast to 40% in the unemulsified form; similar results were recorded with vitamin A.

These investigations indicate clearly that particle size plays an important role in the absorption of fat and vitamin A in premature infants. In these investigations the maximum reduction in particle size was not achieved, and with further improvements and refinements in emulsification even more satisfactory results may be obtained. *Jas. M. Smellie*

1519. **Experiences with Oral Administration of Streptomycin in Enteritis and Intoxications in Infancy.** (Erfahrungen mit oraler Streptomycinbehandlung bei Enteritiden und Intoxikationen im Sauglingsalter)
E. MARTISCHNIG. *Österreichische Zeitschrift für Kinderheilkunde und Kinderfürsorge* [*Öst. Z. Kinderheilk.*] **5**, 272–283, 1950. 3 figs., 13 refs.

The author reports observations made on 43 infants whose ages varied from 2 to 12 months, 20 of whom suffered from gastro-enteritis and 23 from toxicosis. They were all treated orally with streptomycin, only 2 receiving intramuscular injection in addition. The daily dose was divided into 5 or 6 equal parts, and was given in solution in water (100,000 μg. per ml.). During the first 2 days the infants were given 150,000 μg. per kg. body weight to prevent the development of resistance in the causative organisms. If no success was noticed after 6 to 8 days, or after 10 days at most, the treatment was discontinued. In addition the children were subjected to the usual routine treatment. Those with an infective enteritis and with intestinal intoxication were cured, but 5 infants died whose toxic condition was due to a secondary infection involving either the middle ear, the lungs, or the bladder. In comparing these figures with those of previous years the author comes to the conclusion that streptomycin has a definite value in all uncomplicated cases of bowel infection, even with symptoms of intoxication, but not in parenteral diarrhoea. In examining the faeces bacteriologically to study the effect of streptomycin on *Bacterium coli* the author found that the cultures for the most part became sterile. Investigations with the electron microscope showed that low concentrations of streptomycin in contact with *Bact. coli in vitro* had only a bacteriostatic effect, but higher concentrations exerted a bactericidal action.
Franz Heimann

1520. **A Study of the Occurrence of Normal Rh-Negative Infants Born to Sensitized Rh-Negative Women**
S. P. LUCIA and M. L. HUNT. *Journal of Pediatrics* [*J. Pediat.*] 37, 599–603, Oct., 1950. 10 refs.

The authors selected, from amongst 250 cases of Rh sensitization investigated at the University of California Medical School, 30 in which normal Rh-negative infants were born. Tables are given indicating the results of the serological tests and details of previous children. The cases fall into two groups: (1) in which the Rh antibody was present in every examination, and (2) in which it was present in some examinations, but not in all. The first group was further divided into those cases in which the titre of antibody rose by at least two dilutions, and those in which it remained constant. In those showing an increase in titre, appreciable amounts of antibody were found in all cases, both in saline and albumin. In those with a constant titre, 7 out of 10 showed an appreciable amount of antibody and in 6 out of 8 this was present in saline and albumin. In the second group of cases titres were low in all, but were present in saline and albumin in 7 out of 13 cases.

The authors attribute the rising titres to an " anamnestic " reaction occurring during pregnancy, and the constant titres as being due to carry-over from a previous sensitization. In the latter group, however, they found greater ABO incompatibility between mother and child than might have been expected, and the failure of the titre to rise might be due, in their opinion, to competition of antigens. *H. G. Farquhar*

1521. **Essential Enuresis: Successful Treatment based on Physiological Concepts.**
N. D. CROSBY. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 533–543, Oct. 7, 1950. 4 figs., 40 refs.

Essential enuresis is defined as the involuntary and unconscious passing of urine, after an arbitrary age limit of 3 years, in the absence of significant congenital or acquired defect or disease of the nervous or urogenital systems and in the absence of significant psychological defects. The author contends that as the child grows the conversion from the normal enuresis of infancy to continence usually occurs by physiological processes and that a later reversal from continence to enuresis is always possible. In health the conversion process to the establishment of continence develops because a " wet urinous state " (somatic discomfort) acts as an inhibitory stimulus and gives rise to an unconditioned response tending to inhibit continuation of urination by inhibiting the detrusor and contracting the vesical sphincter. This natural conversion process may be reinforced by some training methods, but more often there is a danger that these artificial methods will interfere with the natural process and even make the condition worse. The simple type of essential enuresis is that in which the diurnal and nocturnal volumes of urine passed are relatively normal, but the bladder tension initiates micturition before the discomfort of the distended bladder reaches the threshold to disturb sleep. This, however, is often complicated by superimposed conditioned responses which initiate micturition.

In all the cases studied the urine was collected for at least 3 days, the times and volumes were recorded, and a " urinary pattern " charted. In none was the night volume of urine abnormally large.

The aims of treatment were to extinguish any conditioned responses which initiate micturition and to reinforce the natural method of building up the " inhibitory " tone which is considered necessary for continence. For this purpose a special electrical apparatus

was devised which the child wore at night. Thus, when the patient urinated during the night time he received an electric shock through electrodes applied to the loins. At the same time light and sound signals were made to the observer (parent or nurse). During the day the child led a normal life and no dietary or fluid restrictions were imposed. No other form of treatment was used and the results obtained closely paralleled those encountered with the classical experiments on conditioned responses. A total of 52 patients were given treatment on these lines and a cure was effected in 46. The least number of stimuli required to produce continence was 5, but the majority of the children needed 15 to 40 stimuli.

Jas. M. Smellie

1522. **Simulation of Cardiac Disease by Adrenocortical Failure in Infants**

L. H. KYLE and C. Q. KNOP. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 681–690, Nov. 2, 1950. 7 figs., 29 refs.

The authors report 3 cases of fatal illness in young infants (in one family) in which the cause of death is believed to have been adrenocortical hyperplasia with adrenocortical failure. In 2 of the cases the presenting symptom was cardiac collapse, with a slow and irregular pulse. These were the second and third cases of the series and were observed in hospital. It was in the third that the possibility of adrenocortical failure was considered; this diagnosis was confirmed during life by the high potassium level in the blood, by the increased urinary excretion of 17-ketosteroids, and by a significant improvement in the clinical condition after giving deoxycortone; and after death by the finding of a " greatly enlarged " adrenal cortex.

The paper includes a critical discussion of the recent literature and case records of adrenal insufficiency in infancy. Its clinical symptoms may be either gastrointestinal and suggestive of pyloric stenosis; or cardiac, with a slow and irregular pulse, and suggestive of congenital cardiac disease. Congenital adrenal hyperplasia is familial, producing always in females, but seldom in males, obvious genital abnormalities. Although adrenal failure does not occur in all cases, this is commoner in male infants. The diagnosis of adrenocortical hyperplasia with adrenocortical failure should be considered in all seriously ill infants with genital abnormalities, especially if there is a family history of genital abnormalities or of unexplained deaths in infancy.

C. McNeil

1523. **Progeria (Hutchinson–Gilford Syndrome). Report of a Case and Review of the Literature**

J. THOMSON and J. O. FORFAR. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **25**, 224–234, Sept., 1950. 13 figs., bibliography.

A case of what is claimed to be " classical " progeria is described. The diagnostic criteria are specified, and a list of 18 accepted cases is given. The main findings in these 18 cases are given in a table. Brief reference is made to 24 atypical cases. Gorter, in 1942, describing one of these, suggested the name " progeroid " for them, while Gilford thought that the clinical picture was modified by the later age of onset.

The case now described is claimed to be the nineteenth complete case, and the first reported in Britain since 1897. It is of a boy, aged 4½ years, with a relatively large cranium (actually smaller than that for his age), a small face, absence of scalp hair and of eyebrows and eyelashes, 16 teeth, very short clavicles, stunted body growth (height 35 in. (88·9 cm.) compared with a standard 41 in. (105 cm.)), atrophic inelastic skin and wrinkled hands, and general lack of surface fat. The boy showed no obvious lack of intelligence: he was mentally active and excitable, and " if thwarted showed the irascibility of old age ". He had a thin piping voice; extension was limited in most joints, causing a " horse-riding " stance and a straddling gait but allowing him to run " in a rather flat footed manner ". Radiography showed no unusual intracranial calcification and no delay in ossification at the ankles or wrists, or in dental development. There was a loud systolic cardiac murmur: the blood pressure was 106/64 mm. Hg, with no clinical or radiological enlargement of the heart and no hardening of the radial or temporal arteries.

These features are in accordance with those of the other recorded cases of classical progeria. Angina has been reported at the age of 7 years, hemiplegia at the ages of 7 years and of 19 years; in fatal cases there has been evidence before death of general and coronary arteriosclerosis, with coronary occlusion as the most frequent immediate cause of death.

Summarizing the only necropsy findings published (4 cases), the authors suggest that " from the evidence available, the primary defect in progeria is one of pituitary dysfunction. . . . As hyperfunction of the eosinophil cells of the pituitary may produce the changes of acromegaly, it seems logical to deduce that hypofunction of these cells at an early age may produce the characteristic changes of progeria ". *C. McNeil*

1524. **Corpulence or Obesity in Childhood and Adolescence**

H. B. GRAHAM. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 648–659, Oct. 28, 1950. 10 figs., 1 ref.

This is a detailed account of the author's personal approach to the subject of obesity as encountered at four different age periods: in very young children, young children, pubescent children, and adolescents.

Great stress is laid on the psychiatric aspect (both for the parents and the patient) and " the best part of an hour " is needed in each case for the initial consultation. The author pleads for a widespread crusade by paediatricians to guide parents in the training of children in proper eating habits and effective self-discipline.

In addition to verbal advice, certain " temporary crutches " are used: thyroid (up to 7·5 grains (0·5 g.) daily to a child of 7 years), amphetamine, and, for " recognizable gonadal dyscrasias ", endocrine preparations. The main stress, however, is on psychotherapy, physical exercise, and " adequate " thyroid therapy.

[The author's view that obese " young adults " may legitimately consult paediatricians is not one that will meet with universal approval.] *Wilfrid Gaisford*

Medicine: General

1525. **Effect of Salt Deficiency on the Salt Concentration in Sweat**
S. ROBINSON, R. K. KINCAID, and R. K. RHAMY. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 55–62, Aug., 1950. 4 figs., 18 refs.

The daily salt intake and output of 4 young men in good physical condition was measured at Indiana University, the subjects being under full dietary control and the experiments being carried out in an air-conditioned room in which air-movement, temperature, and humidity could be kept constant. Scrupulous care was taken to collect all solids secreted during the experiments, the means used being described. The subjects were unacclimatized, and the object of the experiment was to determine whether or not the reduction in the chloride content of the sweat observed during acclimatization to heat is necessarily due to salt deficiency.

From the results it is concluded that men performing daily work in hot environments and sweating heavily may or may not show a gradual decrease in the chloride content of the sweat, depending upon the development of a chloride deficiency. A fall in sweat chloride concentration was observed when 4 to 7 kg. of sweat was secreted daily and the subject's chloride intake was 52 to 203 mEq. daily. This reduction occurred even when the body temperature was raised. When the subjects were exposed to heat stress for shorter periods, so that salt balance was positive, no reduction in the salt concentration of the sweat occurred. By increasing the intake of salt to give a positive balance the salt content of the sweat could be made to increase instead of diminishing on exposure to heat and exercise, while in subjects with a pre-existing salt deficit the salt content of the sweat was reduced even on the first day of the experiment.
A. T. Macqueen

ALLERGIC DISORDERS

1526. **Local Antihistaminic Action**
J. P. HENSEN. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 136–140, Oct., 1950. 11 refs.

Intravenous injections of trypan blue were given to rabbits and intradermal injections of histamine were made into the depilated abdominal skin. Various antihistamine substances made up as ointments in 0·5 or 5% concentration or both were applied to part of the site of these injections and the spread of the dye in treated and untreated areas compared. Tripelennamine, "decapryn", and mepyramine were effective in reducing the area of spread; phenindamine had no effect. Spread was also reduced by intravenous injection of tripelennamine, but not by phenindamine by this route.
V. J. Woolley

1527. **Changes in Tissue Sensitivity associated with Varying Life Situations and Emotions; their Relevance to Allergy**
D. T. GRAHAM, S. WOLF, and H. G. WOLFF. *Journal of Allergy* [*J. Allergy*] **21**, 478–486, Nov., 1950. 7 figs., 4 refs.

In 5 patients urticarial lesions appeared during interviews causing stress. In one patient it was possible to alter the skin response to histamine and pilocarpine from negative to positive by introducing a suitable topic into the conversation. At the same time the skin temperature of the forearm increased by more than 1° C. In 4 physicians who were convinced that eating chocolate caused them to develop migraine, lactose suitably disguised as chocolate caused migrainous headache as often as chocolate. In a patient convinced that minute quantities of milk caused severe indigestion, the mobility of the stomach and duodenum was recorded by balloons. No change of the motility pattern was observed when milk was introduced into the stomach without the knowledge of the patient, but pronounced changes occurred when tap water was used and the patient was told that it was milk. The authors conclude that reactions to an ingested substance cannot be regarded as allergic unless the circumstances of its administration preclude all opportunity for conditioned reflexes to operate.
H. Herxheimer

1528. **Milk Allergy. A Survey of its Incidence; Experiments with a Masked Ingestion Test**
M. H. LOVELESS. *Journal of Allergy* [*J. Allergy*] **21**, 489–499, Nov., 1950. 10 refs.

Questionaries were sent to 191 physicians in New York and district. The replies showed an incidence of allergy to milk (in about 250,000 patients) of 1·5% when judged by clinical standards, and 2·3% when judged by skin tests. A controlled ingestion test is described in which the allergen is masked and a placebo used. In 4 patients with a confirmed history of milk allergy the test was positive in only 2. It is concluded that intracutaneous tests for milk allergy give too many positive results, and that a positive allergic history is not reliable.
H. Herxheimer

1529. **Evaluation of Therapeutic Substances Employed for the Relief of Bronchospasm. VII. Combinations of Diphenhydramine with Ephedrine and Aminophylline**
H. J. RUBITSKY, J. A. HERSCHFUS, L. LEVINSON, E. BRESNICK, and M. S. SEGAL. *Journal of Allergy* [*J. Allergy*] **21**, 559–562, Nov., 1950. 3 figs., 2 refs.

Attacks of asthma were induced by the intravenous injection of either 0·01 to 0·05 mg. of histamine or 0·1 to 0·5 mg. of methacholine, the reduction of the vital capacity being recorded. The protective effect of a test substance was estimated by its ability to prevent this

reduction of the vital capacity. Combinations of 50 mg. diphenhydramine (" benadryl "), 25 mg. ephedrine, and 200 mg. " aminophylline ", given orally, had usually no more effect than the most potent single ingredient, whether two or three substances were given together. Aminophylline with diphenhydramine was an exception, but in this case also the increase in effect did not approach arithmetic summation. *H. Herxheimer*

1530. **The Effect of Ephedrine in Asthma and Emphysema**
A. G. W. WHITFIELD, W. M. ARNOTT, and J. A. H. WATERHOUSE. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **19**, 319–326, Oct., 1950. 1 fig., 12 refs.

The vital capacity and its subdivisions were recorded spirometrically, and the residual air was estimated by means of the hydrogen or helium dilution method in 8 normal and 26 emphysematous subjects. The diagnosis of emphysema was based mainly on the finding of a high ratio of residual air to total lung volume, but also on clinical signs and the presence of dyspnoea on exertion and a chronic cough. A distinction is made between a group of 16 patients assumed to have had no bronchospasm (because they were not asthmatic at the time of examination and no rhonchi were audible) and a second group of 10 others who were wheezing audibly and in whom on auscultation numerous rhonchi were heard. The mean vital capacity in the first group was 2·82, and in the second group 2·11 litres. Ephedrine was given in a dosage of ½ or 1 gr. (32 or 65 mg.) to all subjects, and the measurements were repeated one-half to one hour later. [In the experience of the abstracter the full effect of ephedrine is reached in many cases only after 50 to 60 minutes.]

Ephedrine increased the vital capacity only in the group of emphysematous subjects with audible rhonchi; in these the residual air decreased. The other group (and the normal subjects) showed no change. To 6 patients of this group 2½ to 4 gr. (160 to 260 mg.) of ephedrine was given; this did not affect the vital capacity, but produced severe side-effects.

[The assumption that bronchospasm is absent because rhonchi are absent in the presence of chronic cough is debatable; if the distinction between the 2 groups of patients is omitted, the failure of the authors to demonstrate an ephedrine effect in more than 40% of their cases might be explained by the fact that they have not explored the valuable range of ephedrine dosage from 1¼ to 2 gr. (80 to 130 mg.) in the other 60%.] *H. Herxheimer*

1531. **The Effect of Adrenocorticotropic Hormone (ACTH) and Cortisone on the Course of Chronic Bronchial Asthma**
R. A. CAREY, A. M. HARVEY, J. E. HOWARD, and W. L. WINKENWERDER. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **87**, 387–414, Nov., 1950. 1 fig., 13 refs.

The authors' investigation was confined to cases of severe chronic asthma of 6 months' to 45 years' duration in which there had been constant symptoms for at least 2 months and no relief from any other form of treatment. Adrenocorticotrophic hormone (ACTH) was given daily to 19 patients; the dose was initially 100 mg., and was gradually reduced, treatment being continued for periods varying from 4 to 21 days. In 15 of these patients there were complete subjective and objective remissions; the other 4 improved by 50% or more. Improvement was noted within 36 hours in all cases and often within 4 hours. The duration of complete remission varied from 3 days to 10 months, with an average of 68 days. In no case was relapse as severe as the original attack. Second courses of ACTH were given 6 to 224 days after a relapse, response being as prompt and complete as after the first course.

Cortisone was less effective. In 1 case of mild asthma there was a remission which lasted 51 days after 300 mg. of cortisone for 2 days followed by 200 mg. for 9 days, but 4 more severe cases responded only partially to 200 mg. on the first day and 200 mg. daily for the next 7 days. Three cases also failed to respond subsequently to full doses of ACTH, in spite of a fall in the eosinophil count and an increase in 17-ketosteroid excretion. The eosinophil count fell by 72% or more in all except 2 cases, but a significant fall did not ensure improvement in the asthma nor did the absence of a significant fall preclude it. Complete freedom from symptoms usually occurred on the day of maximum response. The duration of the eosinophil response was no indication of the duration of remission. Skin sensitivity was partially or completely abolished during treatment, but tended to re-appear a few days later.

The authors believe that once the likely duration of remission for any one patient has been determined, intermittent courses of ACTH may keep the condition under continuous control. *Robert de Mowbray*

1532. **Intramural Dissemination of Spores of *Hormodendrum resinae***
C. M. CHRISTENSEN. *Journal of Allergy* [*J. Allergy*] **21**, 409–413, Sept., 1950. 1 fig., 1 ref.

Spores of the mould, *Hormodendrum resinae*, were liberated in a room on the first floor of a four-storey building. Within a few minutes the spores could be traced in all rooms of the second, third, and fourth floors, the doors of which were open. Very few spores could be found 12 hours later. The latter finding is probably due to the fact that efficient circulation of air through the building carried most of the spores into the open. *H. Herxheimer*

METABOLIC DISORDERS

1533. **ACTH and Colchicine in the Clinical Treatment of Acute Gouty Arthritis. Physiological Considerations and Review of Therapeutic Results in Fifty-one Attacks**
B. Q. WOLFSON, H. D. HUNT, C. COHN, W. D. ROBINSON, and I. F. DUFF. *Journal of the Michigan State Medical Society* [*J. Mich. med. Soc.*] **49**, 1058–1064 and 1083, Sept., 1950. 1 fig., 18 refs.

Adrenocorticotrophin (ACTH), given in doses small enough to be free from undesirable effects, will end almost all acute attacks of gout within 24 hours. When

the hormone is withdrawn some patients relapse within a few days, but this is found to be prevented by the simultaneous administration of colchicine. In this study three preparations of ACTH were used: (1) aqueous ACTH; (2) a long-acting preparation of ACTH adsorbed on colloidal aluminium phosphate; and (3) a new long-acting preparation named " polyvinyl-adactar " (ACTH adsorbed on aluminium phosphate in polyvinyl-pyrrolidone).

Patients treated with the first two preparations received an initial dose of 50 mg. which was repeated at 6-hour intervals until 75 to 90% improvement was observed. Administration of colchicine was started at the same time in a dose of $\frac{1}{100}$ grain (0·65 mg.) 4 times daily, which was continued until diarrhoea occurred, when it was stopped; with recovery from the diarrhoea it was resumed at a lower dosage, the process being repeated until the maximum daily dose which was well tolerated was ascertained, and this was continued for at least 2 weeks after all residual joint soreness had disappeared. The results of eosinophil counts in the peripheral blood, taken before, and 4 hours after, each dose of ACTH, and determinations of the urine urate/creatinine ratio in 1-hour urine samples taken before, and during the 4th hour after, each dose suggest that a good therapeutic response is not obtained until ACTH evokes a good increase in adrenal function. Clinically, little change is noted for 2 to 3 hours after the initial 50-mg. dose of ACTH. Then, in patients who respond well, subsidence is rapid. In other cases there may be no change until the second or third dose is given, when there may be either the same rapid improvement or a more gradual recession. The emotional state which commonly precedes and accompanies acute gout is dissipated as rapidly as the joint symptoms. In a series of 38 attacks treated by the authors 75 to 90% improvement was generally obtained within 24 hours.

Patients treated with polyvinyl-adactar were given an initial dose of 100 mg., which was repeated at 24-hour intervals until 75 to 90% improvement was noted. This preparation appears to be active up to 48 hours after a single dose. Colchicine was given simultaneously in the manner already described. Of 13 attacks treated (5 not previously treated with colchicine, 8 colchicine-resistant attacks), all but one were terminated by a single injection of the ACTH preparation, and in 11 of the attacks 75% improvement was apparent at the end of 12 hours.

Kenneth Stone

1534. **Respiratory Acidosis in Children with Cerebral, Pulmonary and Cardiovascular Disorders**

D. E. JOHNSTONE and E. BRUCK. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 578–599, Oct., 1950. 1 fig., 21 refs.

Full details of the clinical picture and results of investigations in 16 cases of respiratory acidosis seen at the Children's Hospital, Buffalo, New York, are reported in this paper. The authors divide the conditions causing retention of carbon dioxide into four main groups: (1) Conditions in which respiration is depressed owing to cerebral damage (from trauma, infection, or drugs) or to pulmonary conditions such as increased intrathoracic pressure, loss of lung elasticity, or pleuritic pain. (2) Disorders affecting the respiratory function of the alveoli, such as emphysema, inflammatory oedema, and congenital dysplasia. (3) Conditions in which carbon dioxide cannot escape from the alveoli owing to obstruction by foreign body or oedematous mucous membrane. (4) Inefficient pulmonary blood flow, as in some congenital cardiac disorders.

The diagnosis of respiratory acidosis is dependent on the findings of a low *p*H together with a high carbon dioxide tension in the plasma. In 7 of the cases reported the *p*H was below 7, in one case being as low as 6·89. Details of the techniques employed are given, the authors recommending that arterial blood or blood from the internal jugular vein, returning directly from the respiratory centre, be used.

The compensatory mechanisms which protect the body from changes in *p*H, including the chloride shift from plasma to erythrocytes, the increased excretion of chloride in the urine, and the further increase in plasma bicarbonate level, are discussed.

Treatment should be directed first to the relief of the cause of respiratory acidosis. Symptomatic relief may be obtained by the administration of sodium bicarbonate or sodium lactate, the amount of bicarbonate to be given being calculated from the Henderson–Hasselbalch equation. Frequent estimations of *p*H and alkali reserve during treatment are essential. *R. M. Todd*

1535. **Asymptomatic Hyponatremia in Pulmonary Tuberculosis**

E. A. H. SIMS, L. G. WELT, J. ORLOFF, and J. W. NEEDHAM. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1545–1557, Nov., 1950. 4 figs., 27 refs.

This investigation was carried out at Yale University School of Medicine, and its purpose was to find out why patients suffering from pulmonary disease sometimes have low serum sodium levels. Ten patients of both sexes, aged between 43 and 63 years, were studied; 9 of them had advanced pulmonary tuberculosis and one miliary tuberculosis. All were severely undernourished, with loss of weight, low serum protein level, and low blood pressure, and most of them had other diseases at the same time, such as carcinoma or arteriosclerosis. On ordinary hospital diet with a free intake of salt these patients had a low serum sodium level, but they excreted large amounts of sodium in their urine. When 6 were made to eat large amounts of salt the serum sodium level remained low, though slight increase was generally noted; their urinary excretion of sodium, however, became very high. When 5 patients were given very small amounts of salt to eat their excretion of sodium was low. Symptoms associated with salt depletion were usually absent. Intravenously injected sodium was retained normally. The renal clearances of these patients were normal, though somewhat on the low side, and there was no other evidence of kidney failure. The response to deoxycortone, moreover, was normal—namely, a reduction in salt excretion. All this suggests that the kidney tubules were able to reabsorb sodium and that renal

failure could not have caused this syndrome. There was no evidence of adrenocortical insufficiency either clinically or in various tests, and the adrenal cortex was normal in the 6 patients who ultimately came to necropsy. The total amount of extracellular water was apparently normal and this may explain why symptoms usually associated with salt depletion were absent. All the evidence taken together suggested that the cause of the disturbance was in the cells of the body, and the hypothesis is guardedly put forward that a reduction of the osmotic pressure in the cells was followed by a lowering of the osmotic pressure of all body fluids. The authors also present some evidence to suggest that a lowering of the serum sodium level is not directly associated with tuberculosis, but that it may be present in any severe illness with malnutrition.

E. M. Glaser

1536. **A Study of Obesity by Provocation of Diuresis and Measurement of the Lipocytic Quotient.** (Étude physio-pathologique de l'obésité par les épreuves de diurèse provoquée et le coefficient lipocytique)
M. Albeaux-Fernet, J. Hervé, and M. Corteville. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 4418–4422, Nov. 18, 1950. 13 refs.

A series of 16 patients suffering from obesity were subjected to a 4-hour test of water elimination after drinking 600 ml. of water. This test was carried out on two occasions in each case, the first with the subject lying down, the second with the subject up and about. In addition, the ratio of the plasma cholesterol level to that of fatty-acid (" lipocytic quotient ") was estimated in each case. There was a considerable degree of water retention in all cases, which was more marked in the ambulant test, while the lipocytic quotient was low in all cases, ranging from 0·30 to 0·40 (normal 0·43 to 0·45).

H. K. Goadby

1537. **An Effect of Vitamin B_{12} on Pain in Nutritional Neuropathy**
W. B. Bean, M. Franklin, and A. L. Sahs. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 431–434, Oct., 1950. 11 refs.

Vitamin-B_{12} concentrate was administered to 3 patients suffering from malnutrition and peripheral neuropathy. The first patient was a man aged 43, addicted to alcohol and suffering from pain in the lower limbs. Pain and paraesthesiae were so severe that the patient was unable to walk. Whereas an intramuscular injection of 1 ml. of normal saline was without effect, an injection of a similar quantity of liquid containing 15 μg. vitamin B_{12} relieved the pain within half an hour, and walking was resumed without difficulty. When the pain recurred the placebo was again ineffective and the vitamin injection again allayed the pain, although the beneficial effect was less pronounced than on the first occasion. A successful result was also obtained in a girl aged 17 with malnutrition of obscure aetiology. She suffered from pain in the extremities which was rapidly relieved after the administration of vitamin B_{12}. In a case of chronic alcoholism with a history of pain in the legs and feet of 5 years' duration a single injection of vitamin B_{12} relieved pain in 1 hour and there was no recurrence during the subsequent 2 weeks.

The injection of vitamin B_{12} failed to relieve pain due to anterior poliomyelitis, rheumatoid arthritis, ruptured intervertebral disk, and other disabilities not attributable to malnutrition. The effect of vitamin B_{12} in the cases of malnutrition was considered to be a direct one and not due to increased absorption from the alimentary tract. Nor was the effect due to sedation, for vitamin-B_{12} administration produced no change in the pain threshold of 2 normal subjects. It is suggested that the effect of the vitamin is to increase the blood flow through the nutrient arteries of the nerves. Evidently further investigation is required in order to determine the exact mechanism.

A. Garland

1538. **Clinical Recognition and Treatment of Acute Potassium Intoxication**
J. P. Merrill, H. D. Levine, W. Somerville, and S. Smith. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 797–830, Oct., 1950. 11 figs., bibliography.

Nine cases of potassium intoxication in patients with oliguria or anuria were studied at the Peter Bent Brigham Hospital, Boston, Massachusetts, 2 of the patients dying from potassium intoxication and one from the underlying disease, and 6 patients recovering. Typical electrocardiograph changes were noted in all cases, tall, pointed T waves and prolongation of systole being the first to appear, leading on to auricular fibrillation or standstill, intraventricular block, bundle-branch block, and extrasystoles. Finally, in the fatal cases, there was ventricular fibrillation or ventricular standstill. The electrocardiogram is considered by the authors to provide the best way of determining the severity of potassium intoxication and also the best way of diagnosing this condition before other signs become apparent. The concentration of potassium in the blood, however, was not clearly correlated with either the clinical picture or the electrocardiogram, and patients with a low serum sodium level appeared to be more ill than those with normal serum sodium.

Treatment by the intravenous administration of calcium salts had no effect. The therapeutic effects of testosterone were doubtful, and those of intravenous infusions of sodium salts slight. The authors found that the treatment suggested by Bywaters on theoretical grounds, notably the administration of glucose and insulin, was usually effective, but they consider the best form of treatment to be by dialysis of the blood through an artificial kidney since it enables the administration of glucose and sodium to be combined with the removal of potassium and metabolites. Cation-exchange resins by mouth were also given and seem to have had some beneficial effect.

E. M. Glaser

1539. **The Significance of Pyralgia and Certain Signs in Africans**
N. L. Corkill, H. Creditor, and G. E. S. Stewart. *Journal of Tropical Medicine* [*J. trop. Med. Hyg.*] **53**, 201–208 and 215–226, Oct. and Nov., 1950. 3 figs.

DIABETES

1540. **Diabetic Physicians**
R. F. BRADLEY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 444–447, Oct. 7, 1950. 6 figs., 5 refs.

The author discusses at some length the various problems that may arise when a physician develops diabetes. It is estimated that 1 in every 40 physicians is a diabetic, and that he may expect to live but a few months less than his non-diabetic colleague and considerably longer than his non-medical fellow sufferer. The author suggests that medical schools should accept for training all diabetics who show no degenerative changes as a result of their disease, have not had the disease for more than 15 years, and can demonstrate that they are able to maintain good control of the disease. The onset of diabetes in a young physician is not considered to be a sufficient cause for his giving up his occupation, though the occurrence of frequent hypoglycaemic attacks in a surgeon might force him to change to another branch of medicine. The author stresses the importance of weight control in preventing the onset of the complications of diabetes. *G. S. Crockett*

1541. **Insulin Resistance. Review of the Literature and Report of a Case associated with Carcinoma of the Pancreas**
J. K. DAVIDSON and E. E. EDDLEMAN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 727–742, Nov., 1950. 43 refs.

In reporting, from Emory University and Grady Memorial Hospitals, Atlanta, Georgia, the case of a 49-year-old negress who was found to be " insulin resistant " the authors adopt the arbitrary definition of this condition as " a state which requires 200 or more units per day for longer than 48 hours for regulation in a nonacidotic person with diabetes mellitus ".

In the case reported, the patient required 215, 680, and 340 units of soluble insulin respectively on three successive days after her second admission to hospital. Ketones were found in her urine only intermittently during this time, though on both the first and the second admissions to hospital large quantities of insulin were required during the first few hours of treatment to eliminate ketosis. On her third admission she was found to require 9,600 units of soluble insulin over a 17-hour period before the urine became ketone-free. Subsequently she became comatose and died 27 hours after admission. Necropsy showed a carcinoma of the body of the pancreas with metastases in the liver.

Serum was obtained from the patient on several days before her death, but attempts to demonstrate insulin-neutralizing antibodies by Lowell's technique failed. The authors suggest that this failure may have been due to the large amount of circulating insulin present.

The literature on the subject of insulin resistance is reviewed and details of 50 cases which fulfilled the criteria given above are summarized. The serum of 26 of these recorded cases had been tested for circulating antibodies and positive results had been obtained in only 9 cases. No fundamental relationship existed between resistance and insulin allergy, and no single disease or pathological process appeared to be responsible for the resistance. A wide variety of associated diseases were present, including haemochromatosis and thyrotoxicosis.

[This is a good review of the subject of insulin resistance. The present case, however, only satisfied the authors' strict criteria for 3 days; during the remainder of the time she was in diabetic acidosis, which alone would cause refractoriness to insulin therapy.]

I. McLean-Baird

1542. **A Hyperglycemic Factor Extracted from the Pancreas**
I. J. PINCUS. *Journal of Clinical Endocrinology* [*J. clin. Endocrinol.*] **10**, 556–571, May, 1950. 7 figs., bibliography.

There is no conclusive evidence that a hyperglycaemic factor of the pancreas has any physiological role, but contributory evidence is suggestive enough to warrant review.

Large doses of insulin are not required in man after total pancreatectomy, 40 units per day being usually sufficient, while the insulin requirement of diabetics is not increased after this operation. Experimental diabetes produced in dogs by giving anterior pituitary extract is characterized by great hyperglycaemia and insulin resistance; pancreatectomy produces a fall in blood sugar level, a decrease in insulin requirement, and insulin sensitivity. Similar differences are found between diabetes produced in dogs by subtotal pancreatectomy or alloxan and that produced by total pancreatectomy. These and other clinical findings could be explained by the presence of a substance raising the blood sugar level (and perhaps also decreasing ketosis).

Such a hyperglycaemic substance has been extracted from the pancreas after alloxan treatment or duct ligation and so is presumably derived from the α-cells of the islets. It is a protein which is very difficult to separate from insulin; most commercial preparations of insulin and even crystalline preparations have it as a contaminant. Such preparations produce a slight hyperglycaemia before the hypoglycaemia is produced. When the insulin is inactivated by heat and alkali the full hyperglycaemic activity is revealed. The substance also stimulates glycogenolysis in isolated liver slices. This is probably its mode of action in the body since the hyperglycaemic action is shown best by intravenous or intraperitoneal injection: when given by subcutaneous or intramuscular injection the effect is very small. In addition the substance is ineffective after the liver glycogen has been depleted by starvation or after hepatectomy.

Peter C. Williams

1543. **Statistical Study of 6,000 Cases of Diabetes**
H. J. JOHN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 925–940, Oct., 1950. 7 figs., 4 refs.

See also Section Genetics, Abstract 1360; and Section Cardiovascular Disorders, Abstract 1581.

Cardiovascular Disorders

1544. **Nonspecific Benign Pericarditis**
W. B. PORTER, O. CLARK, and R. R. PORTER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 749–753, Oct. 28, 1950. 5 figs., 7 refs.

Cases in the literature are reviewed and the authors also quote 219 patients with acute pericarditis of whom 14 were diagnosed as having non-specific benign pericarditis. It is noteworthy that the possibility of coronary thrombosis was considered in every case.

This essentially benign disease with a good immediate and ultimate prognosis must be distinguished from myocardial infarction. In the former a friction rub is present at the beginning of the illness and lasts a week or more; in the latter it occurs 2 or 3 days after the onset of the pain and is typically transient. The pain in the former is intermittent, may last for 2 or 3 weeks, and is aggravated by deep inspiration, rotation of the trunk, and by swallowing; in the latter it is of shorter duration and is not aggravated by these factors. Leucocytosis, raised erythrocyte sedimentation rate, and pyrexia are found at the onset of the pain in benign pericarditis, but develop after the onset of the pain in the case of infarction. In benign pericarditis serial electrocardiograms invariably show a return to normal, and there is temporary increase in the size of the cardiac shadow. Electrocardiographic changes tend to persist in cases of myocardial infarction, and there is commonly an absence of cardiac enlargement in this condition.

Geoffrey McComas

CARDIOGRAPHY

1545. **Auricular Flutter Studied in Direct Leads from the Human Heart**
F. M. GROEDEL and M. MILLER. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 183–188, Oct., 1950. 1 fig., 17 refs.

A patient with mitral stenosis and impure auricular flutter was subjected to mitral commissurotomy. The opportunity was utilized to explore electrocardiographically the exposed left auricle. The results obtained suggested that polyfocal stimulation of the left auricle was responsible for the rhythm. *Paul Wood*

1546. **Electrocardiographic Study of Intramuscular Quinidine Lactate**
J. S. FEIBUSH and D. GREENBERG. *American Heart Journal* [*Amer. Heart J.*] **40**, 585–589, Oct., 1950. 1 fig., 8 refs.

Quinidine lactate was given intramuscularly to 10 patients with uraemia and to 5 other patients with various diseases, but without renal failure, in a dosage of 6·5 mg. (0·1 ml.) per kg. body weight. Electrocardiograms were taken a quarter of an hour and 1, 2, 4, and 8 to 12 hours after the injection and compared with those taken before the injection (which, in the former group, were all abnormal). In analysing the results, it was noted that the earliest effect of quinidine (at 15 minutes) consisted in a prolongation of the Q–T interval and depression of the T wave. These changes usually appeared simultaneously, but the T-wave change disappeared sooner than that in the Q–T interval. The patients with normal renal function showed the same electrocardiographic changes in response to the quinidine injection and in some cases they lasted as long as 11 hours. It is stated in a short addendum that quinidine gluconate has an identical effect. *A. I. Suchett-Kaye*

1547. **Normal Esophageal and Gastric Electrocardiograms. Description, Statistical Analysis and Bearing on Theories of " Electrocardiographic Position "**
A. D. KISTIN, W. D. BRILL, and G. P. ROBB. *Circulation* [*Circulation*] **2**, 578–597, Oct., 1950. 7 figs., bibliography.

Electrocardiograms from 15 oesophageal and gastric leads, standard limb leads, 6 precordial leads (V_1 to V_6), and augmented unipolar extremity leads were recorded in 50 normal males. Previous observations were confirmed that P waves with an intrinsic deflection are obtained when the exploring electrode is in a position opposite the left atrium; such positions (atrial levels), ranged from 32·5 to 47·5 cm. from the nares, there being some tendency for a trial level to vary with the height of the individual, but in all but one case an atrial lead was obtained at 40 cm. from the nares. The electrode positions from which ventricular leads were obtained lay in the lowest few centimetres of the thoracic oesophagus or in the stomach, leads from the intermediate positions between atrial and ventricular levels being termed " transitional ". Evidence was obtained that an electrode in the lower part of the oesophagus may occasionally be over the right ventricle in normal individuals.

In the atrial leads P consists of a small initial deflection followed by a diphasic complex which is most often inverted, sometimes upright, and occasionally diphasic. The interval from the beginning of the small initial deflection of P to the beginning of the upstroke of the main diphasic complex varied from 0·01 to 0·05 second (mean $0·03 \pm 0·01$). The interval from the beginning of P in the atrial leads to the onset of the intrinsic deflection (representing approximately the time from the first atrial activity in the atrial leads to activation of the myocardium closest to the electrode) ranged from 0·03 to 0·08 second (mean $0·056 \pm 0·013$). Study of the Q wave in transitional and ventricular leads suggested that the existing criteria for the size of the normal Q in these leads are inadequate and misleading. Previous observations were confirmed that the base of the left ventricle is a region of late activation. In most of the cases in this

series aV_F was very much like the ventricular leads, but there were important exceptions which suggested that the predominant potentials contributing to the resultant recorded as aV_F may be derived from a more extensive region than that which contributes to the ventricular leads. In ventricular leads T is usually positive, but may be diphasic or inverted, in normal subjects. Marked RS–T deviation was recorded in oesophageal and gastric leads. Some of the current assumptions, but not all, about the " electrocardiographic position " of the heart were confirmed. For instance, the evidence presented contradicts Goldberger's theory that RS complexes with no Q wave in precordial leads are only derived from electrodes in positions over the right ventricle.

[This carefully documented article should be read in the original. Full justice cannot be done to it in an abstract.] *William A. R. Thomson*

1548. **Left Ventricular Cavity Potentials in Induced Left Bundle Branch Block Studied with Esophageal Leads**
A. A. SANDBERG, J. WENER, and L. SCHERLIS. *American Heart Journal* [*Amer. Heart J.*] **40**, 531–544, Oct., 1950. 6 figs., 35 refs.

A very unusual case of induced left bundle-branch block (L.B.B.B.) in a woman of 43 suffering from angina of effort is reported. Progressive transition from normal conduction to L.B.B.B. and vice versa was recorded electrocardiographically by means of simultaneous precordial, standard, and oesophageal leads, this last reflecting left ventricular cavity potentials. The L.B.B.B. was seen to occur when the patient performed a standard exercise test or after the inhalation of amyl nitrite, but only when the heart rate increased until the R–R interval was 0·57 second, compared with 0·75 second before the test. After 33 seconds, at which time the R–R interval was 0·63 second, the pattern abruptly changed from that of L.B.B.B. to that of normal conduction. The transition from normal conduction to L.B.B.B. and back was thus associated with a critical heart rate. The electrocardiographic changes in the oesophageal leads consisted in the appearance of an equiphasic RS pattern replacing the normal QS pattern; the RS–T segment was depressed and the QRS duration during L.B.B.B. measured 0·10 to 0·11 second, which is in favour of an incomplete L.B.B.B.

A. I. Suchett-Kaye

1549. **The Course of the Excitation Wave in Patients with Electrocardiograms Showing Short P–R Intervals and Wide QRS Complexes (Wolff–Parkinson–White Syndrome). An Analysis Based on Studies with Intracardiac and Esophageal Leads**
A. GRISHMAN, I. G. KROOP, and M. F. STEINBERG. *American Heart Journal* [*Amer. Heart J.*] **40**, 554–572, Oct., 1950. 10 figs., 23 refs.

In 7 patients with Wolff–Parkinson–White electrocardiograms, the course of the excitation wave has been explored by means of intracardiac and oesophageal leads. The findings strongly suggest that the excitation wave originates in the sinoatrial node and reaches the posterior aspect of the left ventricle and anterior aspect of the right ventricle simultaneously. The atrioventricular conduction is probably effected by means of accessory muscular pathways. The right ventricular myocardium is stimulated from the epicardial surface toward the cavity. The right ventricular segment of the interventricular septum is stimulated either at the end of the right ventricular excitation or, in some cases, it seems to receive its excitation wave predominantly from the direction of the left ventricle. Atrial flutter was the most frequently observed arrhythmia in these patients during paroxysms of tachycardia. The ventricular complexes remained abnormal or had an exaggerated abnormal appearance, resembling those encountered in ventricular tachycardia. In one instance, nodal tachycardia was recorded with normal ventricular complexes. This would suggest that the excitation wave passed down to the ventricles along the bundle of His in a normal fashion.—[Authors' summary.]

1550. **The Significance of Q_{AVF} in the Diagnosis of Posterior Infarction**
P. N. G. YU and T. M. BLAKE. *American Heart Journal* [*Amer. Heart J.*] **40**, 545–553, Oct., 1950. 15 refs.

In view of the conflict of opinion concerning the clinical value of the unipolar limb leads in the diagnosis of posterior infarction in cases in which a large Q_3 is the only abnormality in the standard-lead electrocardiogram, a comparative and critical study of Q_2, Q_3, and Q_{AVF} was undertaken in 109 cases in which Q_3 was at least 25% of R_3. Of these patients 54 had clinical and electrocardiographic evidence of posterior myocardial infarction, while the remaining 55 had no clinical evidence of myocardial infarction, and their electrocardiogram showed no abnormality of the RS–T segment. A significant Q_{AVF} (voltage 25% of R_{AVF} or more, duration 0·04 second or longer) was demonstrated in all members of the former group (with the exception of one case, in which the diagnosis was confirmed at necropsy), but in only 3 of the latter group. A measurable Q_2 was found in three-quarters of the former group, its voltage being at least 25% of R_2 in one-half of these.

It is concluded that the mere presence of a deep Q_3, with or without an inverted T_2, is not a reliable diagnostic sign of posterior myocardial infarction, and that while the finding of a significant Q_2 is definitely helpful in the diagnosis, its absence does not rule out the possibility of a posterior wall lesion; but that the use of the unipolar leg lead can be of real help in the differentiation between the normal and abnormal Q_3 and thus in establishing or excluding the diagnosis of posterior-wall infarction.

A. I. Suchett-Kaye

1551. **The Value of the aV Limb Leads and the V Chest Leads (V4r to V7) in Routine Clinical Electrocardiography**
R. H. ROSENMAN, E. SILBER, L. N. KATZ, and B. SHORR. *American Heart Journal* [*Amer. Heart J.*] **40**, 573–584, Oct., 1950. 2 figs., 14 refs.

1552. **Analysis of H Wave of Ballistocardiogram**
V. DE LALLA. M. A. EPSTEIN, and H. R. BROWN. *Circulation* [*Circulation*] **2**, 765–769, Nov., 1950. 3 figs., 9 refs.

HEART

1553. **The Effect of Digoxin on the Right Ventricular Pressure in Hypertensive and Ischaemic Heart Failure**
R. I. S. Bayliss, M. J. Etheridge, A. L. Hyman, H. G. Kelly, J. McMichael, and E. A. S. Reid. *British Heart Journal* [*Brit. Heart J.*] **12**, 317–326, Oct., 1950. 8 figs., 17 refs.

Changes in the right ventricular pressure after giving 1·0 to 1·5 mg. of digoxin [presumably by intravenous injection] were studied by cardiac catheterization in 15 cases of hypertensive or ischaemic heart disease with left ventricular failure.

Before digoxin, nearly all the patients had a considerably raised right ventricular systolic pressure (26 to 76 mm. Hg) and most a raised end-diastolic pressure (−1 to 21 mm. Hg). The response to digoxin was variable. In 2 cases cardiac output increased significantly, without any significant alteration in the right ventricular pressure. In 10 cases right ventricular pressure fell, the cardiac output rising in 4 of this group and being unchanged in the other 6. In 3 cases right ventricular pressure rose, with a falling or unchanged output and increasing dyspnoea, and in these cases there was a marked rise in systemic arterial pressure (seen to a lesser degree in 5 other cases).

The authors conclude that, except in those cases in which a sharp rise in systemic arterial pressure is produced, digoxin improves the emptying of the failing left ventricle by a direct action on its muscle and so lowers its diastolic filling pressure until, after an increase in left ventricular output for a few beats, the original balance between the output of the two ventricles is restored. The lower left ventricular filling pressure is transmitted through the pulmonary circulation to the right ventricle and may in turn lead to more complete emptying of that chamber and a fall in systemic venous pressure. It is pointed out that such temporary changes in cardiac output could not be recognized by the methods used. The authors consider that this hypothesis accounts more satisfactorily for the observed facts than the previous hypothesis of McMichael and Sharpey-Schafer, of a primary action on venomotor tone.

J. W. Litchfield

1554. **The Pathogenesis of Cardiac Dyspnoea. The Significance, Recognition, and Treatment of a Bronchospastic Component.** (Zur Pathogenese der kardialen Dyspnoe. Bedeutung einer bronchospastischen Komponente, ihre Erkennung und Behandlung)
A. Merkle and F. Wyss. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **80**, 1154–1157, Oct. 28, 1950. 33 refs.

In the experiments described the maximum velocity of expiratory air-flow was estimated in litres per second by means of a new type of pneumometer. The inhalation of 1% *iso*propylnoradrenaline (" aleudrine ") in 10 deep respirations (the " aleudrine test ") did not affect the air-flow velocity in 20 normal subjects. In 50 patients with cardiac failure from different causes—emphysema and bronchial asthma being excluded—and radiologically pronounced pulmonary congestion this test caused an increase in air-flow velocity of 0·3 to 2·6 l. per second without altering the vital capacity. In all but 3 cases the patients experienced relief. It is argued that the small amount of *iso*propylnoradrenaline absorbed (about 50 μg.) could hardly influence the circulation (and in fact pulse rate, blood pressure, and electrocardiogram were unchanged) and that if relief had been due to improvement in the circulation, the vital capacity would have increased. It is therefore concluded that there is an important bronchospastic component amongst the factors causing cardiac dyspnoea.

[Two criticisms might be made: (1) The mean vital capacity of the patients was 1·8 litres, and in some cases it was as low as 0·5 and 0·7 litres; this indicates very severe dyspnoea which would tend to make any respiratory test inaccurate. The tables given show that in those patients with a very low vital capacity (11) the average improvement in air-flow (by 0·66 litres per second) was less than in those with the highest vital capacity (10) who improved by an average of 0·87 litre per second, the mean improvement for the whole group of 50 being 0·77 litres per second. (2) The assumption of the authors that the small absorbed amount of *iso*propylnoradrenaline has no influence on the circulation would appear to require further evidence, as in the abstracter's experience this substance always has some central effect.]

H. Herxheimer

1555. **The Problem of the So-called Isolated Allergic Myocarditis (with Eczema).** (К вопросу о так называемом изолированном аллергическом миокардите (при экземе))
V. P. Kesareva. Архив Патологии [*Arkh. Patol.*] **12**, No. 5, 84–87, 1950. 2 figs., 14 refs.

1556. **Subacute Bacterial Endocarditis: Revision of Diagnostic Criteria and Therapy**
C. K. Friedberg. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 527–534, Oct. 14, 1950. 14 refs.

The author has analysed a series of 148 unselected cases of subacute bacterial endocarditis observed at the Mount Sinai Hospital, New York, since the advent of penicillin in 1944 up to June, 1949. Of these patients 66% recovered. There was not much difference in recovery rate between patients treated in 1944 and those treated subsequently, but 78% of patients below the age of 40 responded to treatment, compared with 52% of those above that age. This may partly be explained by delay in commencing treatment, since all who were seen within 2 weeks of the onset recovered, while half of those in whom treatment was delayed for 3 months died—errors in diagnosis being more liable to occur in older people, in whom anorexia and loss of weight suggest a diagnosis of cancer, or in whom congestive failure may be present and the fever attributed to pulmonary infarction. In almost all the cases in which death was attributed to heart failure, embolism, or uraemia, persistent infection was present. Sensitivity of the organism to penicillin was another factor determining the outcome; the usual sensitivity *in vitro* was between

0·01 to 0·1 unit per ml. and in no case in which it was 1 unit or more per ml. did the patient recover. Patients with a negative blood culture fared badly, partly because treatment was apt to be delayed, and partly because the dosage was more difficult to control.

It is suggested that a tentative diagnosis of bacterial endocarditis should be made in the case of every patient with a cardiac murmur who has had an unexplained fever for over a week. Blood cultures should be made on two successive days and then treatment started. The minimum effective dose of penicillin is 1,200,000 units daily, and if the organism cannot be isolated, a minimum of 2,400 000 units daily should be given. With resistant organisms up to 40,000,000 units may be needed daily, or the effect of penicillin may be enhanced by caronamide. If a Gram-negative bacillus is found on blood culture, streptomycin, 3 g. daily, should be substituted for penicillin. Aureomycin, 3 or 4 g. daily, may be combined with penicillin for staphylococcal or enterococcal endocarditis or with streptomycin for *Brucella* infections.

C. W. C. Bain

1557. **Penicillin Therapy of Subacute Bacterial Endocarditis.** (Пенициллинотерапия затяжного септического эндокардита)

L. K. Kechker. Тераневтический Архив (*Terap. Arkh.*] **22**, No. 5, 23–31, Sept.–Oct., 1950. 3 figs., 17 refs.

The author reports on the effects of penicillin therapy in 46 cases of subacute bacterial endocarditis treated at the First Lenin Medical Institute, Moscow, during the past 2½ years. There were 25 men and 21 women, 19 were between 16 and 30 years old, 15 between 31 and 40 years, and 12 over 40 years old. Of the 39 cases of rheumatic heart disease, in 8 there was mitral, and in 5 aortic valvular disease only, in 25 both mitral and aortic valves were affected, while all the valves were affected in 1 case. Of the remaining 7 patients 2 had syphilitic mesaortitis, 2 congenital heart disease, and 3 patients suffered from primary septic endocarditis. In all cases there were prolonged pyrexia, anaemia, and nephritic symptoms. An enlarged spleen was present in 43 cases, infarction of various organs occurred in 34, endothelial symptoms (splinter haemorrhages, petechiae) were present in 40, and finger-clubbing in 26 cases. Out of 22 cases in which a blood culture was performed only 4 gave a positive result. Penicillin was given intramuscularly at 3-hourly intervals. The author recommends a total dosage of 1,000,000 units in 24 hours for 5 to 10 days; if there is no improvement this dosage must then be increased. The duration of penicillin therapy ranged from 42 to 157 days. The total dosage with which a remission was achieved ranged between 25,200,000 and 288,000,000 units.

Of the 46 patients 20 died, 18 were discharged probably cured, and in 8 cases the outcome is still uncertain. The author suggests that if a remission has lasted for over 6 months a cure has been achieved. Most of the 18 discharged patients have been followed up for over 6 months; 9 are working, 2 studying, one developed heart failure one month after discharge, and one relapsed after 4 months. The others are well but not working yet. The cause of death was heart failure in 8 cases, septicaemia and heart failure in 5, cerebral embolism in 3, septicaemia in 3, and uraemia in one case. The time interval between the onset of the disease and the start of penicillin therapy appeared to be of importance—of 29 patients who were ill for less than 5 months before receiving treatment 13 died, while of 9 who were ill for over 5 months 7 died. The author draws attention to the large number of patients (7) who developed heart failure during penicillin treatment; all 7 died. Out of 10 patients who had heart failure on admission, 4 were cured and 6 died. The importance of good nursing and the elimination of septic foci is stressed.

N. Chatelain

1558. **Speculations on the Mechanism of Cure of Bacterial Endocarditis**

T. H. Hunter. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 524–527, Oct. 14, 1950. 5 figs., 10 refs.

In the treatment of bacterial endocarditis all the responsible bacteria must be killed. Bacteriostatic drugs are useless since the leucocytes cannot deal with bacteria growing in the poorly vascularized vegetations. Penicillin is the only effective drug amongst those now available, but experiments *in vitro* have shown that with strains resistant to penicillin, such as the enterococcus, its effect is enhanced by the simultaneous administration of streptomycin. Penicillin is also most effective against rapidly multiplying bacteria, and in a culture in which the population density is approaching maximum and growth therefore proceeding slowly its early bactericidal effect is not maintained. Addition to such a culture of a mixture of penicillin and streptomycin, however, results in a progressive killing of the bacteria. Clinical trials, in cases of bacterial endocarditis, of combined penicillin and streptomycin therapy over a period of 10 days only have been instituted, and so far the results are stated to have been satisfactory.

C. W. C. Bain

1559. **The Occurrence of Endocarditis with Valvular Deformities in Dogs with Arterio-venous Fistulas**

C. W. Lillehei, J. R. R. Bobb, and M. B. Visscher. *Annals of Surgery* [*Ann. Surg.*] **132**, 577–590, Oct., 1950. 5 figs., 21 refs. [Also in *Proc. Soc. exp. Biol. N.Y.* **75**, 9–16, Oct., 1950.]

Dogs are normally relatively resistant to the development of experimental endocarditis, trauma to the valve combined with the injection of organisms being necessary for its induction. The authors report, however, that 8 out of 10 dogs in whom large arteriovenous fistulae were created developed endocarditis with vegetations spontaneously.

The following factors seem to have a bearing on the development of the lesion: (1) Size of fistula. Large shunts are necessary and smaller ones are ineffective. The development of endocarditis probably depends on the load placed on the heart, which in some cases was estimated to have been increased six-fold. (2) The duration of the load, at least a month being required before even clinical signs of endocarditis appear. (3)

The age of the animal, older dogs being more prone to develop lesions. (4) Bacteriology. No particular organisms have been constantly encountered. Only one animal developed glomerulonephritis, and this was the only occasion in which *Streptococcus viridans* was the causal organism. A further observation of possible significance was the finding of enlargement of the adrenal glands in all cases. *W. P. Cleland*

1560. **Anticoagulants in Treatment of Coronary Thrombosis**
J. A. TULLOCH and A. R. GILCHRIST. *British Medical Journal* [*Brit. med. J.*] **2**, 965–971, Oct. 28, 1950. 5 figs., 43 refs.

The results in 70 cases of myocardial infarction treated with anticoagulants (in addition to other measures) for the first 3 weeks after admission to hospital are compared with those in 84 controls. The cases were unselected and the two groups are shown to be comparable, although treated in different hospital blocks. In all but 6 of the former group intravenous injections of heparin were given 8-hourly initially to maintain a clotting time of 20 minutes (by the Lee–White method) until the prothrombin content of the blood had been reduced to 30% of normal, estimated by Fullerton's method, with dicoumarol by mouth, 300 mg. of which was given on the first day, 200 mg. on the second, and 100 to 200 mg. on the third. Thereafter the dose was determined by the daily prothrombin estimation. The mortality was 40·5% in the control group and 22·8% among those treated with anticoagulants, the difference being significant for the male cases, but not for the female. Thrombo-embolic complications occurred in 24 (28·6%) of the control cases, and in 9 (13%) of the treated cases, being fatal in 13 of the former and 4 of the latter. The duration of bed rest was the same in both series.

The authors conclude that although anticoagulant therapy would reduce the mortality of cardiac infarction by about one-half, either more hospital beds or a laboratory service for the domiciliary control of dosage must be provided before such treatment can be widely applied. *D. Verel*

1561. **Rupture of the Interventricular Septum**
M. J. NAREFF, L. J. SKLAR, F. T. KELLY, and J. R. REULING. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 431–435, Sept. 21, 1950. 5 figs., 13 refs.

DISTURBANCES OF RHYTHM

1562. **Oxygen Therapy of Bundle Branch Block**
J. LEVY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 400–408, Oct., 1950. 7 figs., 29 refs.

The author discusses in detail the aetiology of bundle-branch block. The main cause is disease of the coronary branch supplying the bundle of His. Rheumatic heart disease, diphtheria, syphilis, myxoedema, and digitalis and quinine poisoning are rarer causes, while cases are recorded in the literature of the development of this lesion in apparently healthy young adults. The various factors producing the electrocardiographic (ECG) changes are discussed.

The treatment with oxygen of 3 cases at the Montefrere Hospital, New York, is described in detail. The first was that of a woman aged 59 with angina pectoris and ECG evidence of bundle-branch block. A series of inhalations of oxygen was given for periods of 1 hour with a well-fitting mask, the concentration starting at 40% and quickly increasing to 100%. The ECG showed that the heart block disappeared after 5 minutes' inhalation, although it returned, on removing the mask, after an interval which became gradually longer. A series of experiments are described in which the frequency and duration of the oxygen therapy was varied and the period during which the ECG remained normal was noted. At first 5 daily treatments of an hour each were necessary to keep the ECG normal, but later only 10 minutes daily sufficed. After 5½ weeks all treatment was discontinued and the ECG remained normal, being still normal 6 months later. The second case was that of a woman of 67 with a large variety of symptoms, some referable to the heart, and ECG signs of left bundle-branch block. She was given intermittent oxygen therapy in a tent for 4 days when the ECG reverted to normal and the oxygen was stopped; 11 months later the ECG was still normal. The third case was that of a 75-year-old man with severe oedema, orthopnoea, and angina. ECG showed auricular fibrillation and bundle-branch block. Oxygen was administered, at first with a B.L.B. mask and later in a tent, in addition to digitalis and mercurial diuretics. After several days of oxygen therapy the ECG showed the bundle-branch block no longer to be present and this was maintained. In all 3 cases there was considerable symptomatic improvement apparently attributable to the oxygen therapy. The author records previous reports of the value of oxygen therapy in this condition and mentions also experimental work in dogs supporting the value of this treatment.

[Inhalation of 100% oxygen seems to have had a marked effect in the 3 recorded cases and it appears to be a simple non-toxic treatment well worthy of trial.] *M. H. Pappworth*

1563. **The Modern Pathogenetic Interpretation, Classification, and Electrocardiographic Diagnosis of Disturbances of Intraventricular Conduction. A Study of 175 Cases.** (Moderna interpretazione patogenetica, sistemazione e diagnostica ecgrafica delle turbe della conduzione intraventricolare. Rilievi statistici clinici e radiologici su 175 casi)
D. DE CAROLIS. *Cuore e Circolazione* (*Cuore e Circol.*) **34**, 193–218, Aug., 1950. 9 figs., 42 refs.

The author has studied 175 patients suffering from various disturbances of ventricular conduction from the clinical, electrocardiographic, and radiological standpoints. From this study, and from a review of the literature, he draws a number of conclusions: (1) that clinical and experimental investigations of the last 30 years have undermined the classical concept of bundle-branch block; (2) that the nomenclature of conduction

disturbances is inadequate for present-day needs, because it is related to the electrocardiographic picture of the standard limb leads and to various other criteria, thereby giving puzzling interpretations. A new terminology is suggested, based on radiological and clinical findings and unipolar precordial tracings, which divides disturbances of conduction into "delays" and "blocks". Delays are classified according to the degree of prolongation of the QRS complex and the type of preponderance (left or right). The blocks are divided into right and left intra-ventricular blocks (major and minor), mixed, associated with ventricular hypertrophy, and associated with infarction. It is thought that the electrocardiographic changes do not permit the exact location of the site of the block.

Of the 175 patients examined, 110 had right intraventricular block and 65 had left intraventricular block: 101 of the right-sided blocks were of minor type and 9 were of major type: 27 of the left-sided blocks were minor in type and 38 major in type. There was a marked preponderance of men with both right- and left-sided blocks. Of the patients as a whole 26 had essential hypertension, 36 coronary atheroma, 17 myocardial infarction, 51 a lesion of the mitral valve, 9 cor pulmonale, and 13 a congenital block, and in 23 patients the aetiology was unknown. *F. A. Langley*

1564. **Intravenous Use of Quinidine, with Particular Reference to Ventricular Tachycardia**
A. H. CLAGETT. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 381–388, Oct., 1950. 2 figs., 39 refs.

Although quinidine has been given by mouth in the treatment of ventricular tachycardia since 1922 there are comparatively few references in the literature to its intravenous use. Out of 97 recorded cases, of which 62 were of paroxysmal ventricular tachycardia, in 42 the rhythm reverted to normal and only in 11 cases did reactions occur, 4 of which (all in the same series) were fatal.

In the author's opinion, the intravenous injection of quinidine is justified when rapid action is needed or when the patient is unable to take it by mouth owing to gastro-intestinal upset. He uses ampoules of quinidine lactate containing 0·65 g. in 10 ml. and adds one of these to 50 ml. of 5% glucose, giving the solution intravenously at approximately 2 ml. per minute. Whenever practicable, 0·2 g. is given orally beforehand to test sensitivity. There are two special indications for the intravenous administration of quinidine: (1) in critically ill patients, especially those with ventricular tachycardia in whom oral administration has been ineffective or not tolerated, and those so ill that rapid action is necessary; and (2) during operations on the heart or lungs where cardiac manipulation is likely, the drug being added to the usual intravenous fluid therapy. The author points out that ventricular paroxysmal tachycardia is a frequent and very serious complication of cardiac infarction, and he believes that in such cases intravenous quinidine is not contraindicated as some authors maintain.

The treatment of 13 cases is described in detail. The dose varied from 0·4 g. to 3·25 g., administration being stopped as soon as the rhythm reverted to normal or if toxic symptoms developed. Only 3 patients suffered from toxic symptoms and these were mild (nausea and vomiting). The more severe reactions reported in the literature, such as asystole, convulsions, cyanosis, impaired vision, and unconsciousness, were not encountered in this series and it is suggested that in many of the recorded cases these reactions may have been the result of the disease itself, of the use of impure or too concentrated solutions, or of too rapid administration. Of the author's patients, 4 had paroxysmal ventricular tachycardia and in 3 of these rhythm reverted to normal. One patient with auricular fibrillation and one with flutter also responded favourably. Four cases are described in which intravenous quinidine was given during oesophagectomy for carcinoma; no cardiac irregularity occurred, although there was much cardiac manipulation during the operation. The author maintains that intravenous quinidine therapy as described by him is useful and safe. *M. H. Pappworth*

1565. **Antidotes to Ventricular Fibrillation induced by Mercurial Diuretics**
B. N. CRAVER, F. F. YONKMAN, and B. R. RENNICK. *American Heart Journal* [*Amer. Heart J.*] **40**, 590–594, Oct., 1950. 1 fig., 13 refs.

1566. **Effect of Auricular Fibrillation on Cardiac Output, Coronary Blood Flow and Mean Arterial Blood Pressure**
R. WEGRIA, C. W. FRANK, G. A. MISRAHY, R. S. SIOUSSAT, L. S. SOMMER, and G. H. MCCORMACK. *American Journal of Physiology* [*Amer. J. Physiol.*] **163**, 135–140, Oct., 1950. 3 figs., 3 refs.

Cardiac output and coronary flow were recorded in dogs by means of rotameters. The induction of auricular fibrillation by electrical stimulation of the left or right auricular appendage caused an initial abrupt fall in mean arterial pressure, cardiac output, and coronary flow. After a few seconds all the values tended to return to the control level, the coronary flow in most experiments rising above that level. At the end of the period of auricular fibrillation the arterial pressure, coronary flow, and cardiac output rose to above the control level, the coronary flow remaining high when arterial pressure and cardiac output had returned to normal.

A. Schweitzer

CONGENITAL AFFECTIONS

1567. **Pulmonary Atresia and the Collateral Circulation to the Lungs**
K. D. ALLANBY, W. D. BRINTON, M. CAMPBELL, and F. GARDNER. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **99**, 110–152, 1950. 22 figs., 22 refs.

The clinical and anatomical features in 6 cases of pulmonary atresia are described. In one patient, aged 15, with a closed ventricular septum, the pulmonary circulation was maintained by a widely patent ductus

communicating with a grossly dilated pulmonary artery; the conclusion was reached that the pulmonary blood supply in this instance was better than in many cases of tetralogy. The other 5 cases were of pulmonary atresia with high ventricular septal defect and over-riding aorta. Atresia was usually at, or near, the pulmonary valve, the pulmonary artery being small but patent distal to the atresia. Abnormally large bronchial arteries were found in every case and in some were joined directly with branches of the pulmonary artery. The development and classification of these vessels is discussed. The authors feel that this group of cases with pulmonary atresia should be separated from their conventional classification with the tetralogy and be considered as a distinct entity; only cases with pulmonary stenosis should be defined as the tetralogy of Fallot. On the clinical side the authors make the point that in pulmonary atresia a systolic murmur, generally absent in the pulmonary area, is louder than in the tetralogy. [The article is exceptionally well illustrated and repays close study.] *James W. Brown*

1568. **Apical Diastolic Murmurs in Patent Ductus Arteriosus**

A. RAVIN and W. DARLEY. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 903–914, Oct., 1950. 5 figs., 11 refs.

At the University of Colorado, the authors studied the heart sounds in 21 established cases of patent ductus arteriosus. In 9 cases apical diastolic murmurs similar to those of mitral stenosis were heard. In several of these cases operative correction of the defect abolished the murmur, and in one case of operative death the absence of coincident mitral stenosis was confirmed at necropsy. The occurrence of the murmur seems to be determined by the severity of the disturbance in cardiac hydrostatics caused by the condition. It is suggested that it is produced by what is in effect a functional mitral stenosis: although the absolute size of the mitral ring is normal, its size relative to the ventricular capacity and the rate of blood flow is reduced owing to the effect of the shunt between the aorta and the pulmonary artery.
T. A. A. Hunter

1569. **Effect of the Patent Ductus Arteriosus on the Pulmonary Blood Flow, Blood Volume, Heart Rate, Blood Pressure, Arterial Blood Gases and *p*H**

D. E. CASSELS, M. MORSE, and W. E. ADAMS. *Pediatrics* [*Pediatrics*] 6, 557–572, Oct., 1950. 6 figs., 36 refs.

The authors have studied certain aspects of the circulation before and after ligature of a patent ductus arteriosus. In the 12 cases investigated there was a decrease of 19·6% to 61·8% in pulmonary blood supply following ligation. There was a corresponding decrease in the blood volume in most cases. The heart rate decreased after operation and the pulse pressure diminished, but changes in blood pressure were not always marked despite a general rise in diastolic pressure and a tendency for the systolic pressure to fall a few millimetres. These findings are considered in detail and there is a discussion on the blood gases before and after operation and the possible pulmonary vascular changes which might impede oxygen diffusion. So far there is no positive evidence of such changes, but the possibility cannot be entirely dismissed. *James W. Brown*

1570. **Tracheoesophageal Obstruction from Retroesophageal Patent Left Ductus Arteriosus, with Right Aorta and Other Vascular Anomalies**

H. K. FABER and M. M. GRIFFIN. *Stanford Medical Bulletin* [*Stanford med .Bull.*] **8**, 177–180, Nov., 1950. 1 fig., 7 refs.

A rare type of anomaly of the great vessels is described in which compression of the trachea and esophagus was produced by a vascular ring composed of a right aorta tightly adherent to the pulmonary artery in front and a large patent retroesophageal left ductus arteriosus behind. Brassy cough, respiratory obstruction, and dysphagia were the main symptoms, complicated by recurrent respiratory infection and bronchopneumonia. Tracheal compression prevented the passage of an intratracheal tube for anaesthesia, and consequently prevented operation, which otherwise could have been performed, perhaps with success.

Other anomalies included: separate origin of the four great vessels, the common carotids and the subclavians, the left common carotid arising from the ascending portion of the aortic arch and the left subclavian (with the left vertebral) from the ductus; defects of the interauricular and interventricular septa; and enlargement of the pulmonary artery and right heart. No exactly similar malformation has been found in literature.

Attention is again called to the importance of awareness by the pediatrician and roentgenologist of compressive vascular anomalies as a cause of congenital stridor and other related symptoms and instituting suitable *x*-ray examination, without which the condition cannot be diagnosed. It must not be mistaken for enlarged thymus.—[Authors' summary.]

1571. **Valvular Pulmonic Stenosis with Intact Ventricular Septum and Patent Foramen Ovale. Report of Illustrative Cases and Analysis of Clinical Syndrome**

M. A. ENGLE and H. B. TAUSSIG. *Circulation* [*Circulation*] **2**, 481–493, Oct., 1950. 6 figs., 19 refs.

Three cases of pulmonary valvular stenosis with intact intraventricular septum and patency of the foramen ovale are described. Until recently such cases were diagnosed only in the post-mortem room, but it is now realized that the condition may be distinguished clinically from other types of congenital heart disease. The four most likely conditions with which these cases may be confused are the tetralogy of Fallot, Epstein's anomaly of the tricuspid valve, cor pulmonale, and Eisenmenger's complex. Differential diagnosis is important if operative treatment is contemplated, because patients with this condition seldom do well after a Blalock–Taussig operation, though they may respond well to pulmonary valvulotomy.

The features of importance for the diagnosis of pulmonary valvular stenosis with intact septum are delayed onset of cyanosis, and dyspnoea out of proportion to the degree of cyanosis. These patients seldom squat

when fatigued. On examination they show a precordial bulge and there is evidence of enlargement of the heart, with a pulmonary systolic murmur and weak second sound. The finding of a large and pulsating liver [cirrhosis also occurs] is important because this seldom occurs in other forms of cyanotic heart disease. On fluoroscopy the pulmonary conus is seen to be large and there may be dilatation of the pulmonary arteries, but without increased pulsation. The circulation time is prolonged unless there is a large shunt through the septal defect. Angiocardiography shows delayed emptying of a large right ventricle, but the atrial shunt is usually too small to be distinguished. Heart catheterization demonstrates the pulmonary stenosis, though seldom the patency of the foramen ovale. *H. E. Holling*

1572. **Cor Triatriatum. Concerning the Nature of an Anomalous Septum in the Left Auricle**
C. G. PARSONS. *British Heart Journal* [*Brit. Heart J.*] **12**, 327–338, Oct., 1950. 7 figs., 35 refs.

A male infant, dying at the age of 6 weeks, was found to have a septum dividing the left auricle into an upper and lower chamber. The clinical features noted were tachycardia, marked cardiac enlargement, detectable clinically and radiologically, attacks of cyanosis and dyspnoea, and terminal congestive heart failure. There was no clubbing.

At necropsy, the left auricle was seen to be considerably enlarged and divided into a larger upper and a smaller lower chamber by a thin greyish-white septum which passed almost horizontally from the upper margin of the fossa ovalis to the lateral wall of the auricle just below the opening of the left inferior pulmonary vein. The upper chamber received the four pulmonary veins, and communicated with the lower chamber by a hole, smaller than a pin's head, in the septum. The lower chamber opened into the left auricular appendage and into a hypoplastic left ventricle through a small mitral valve, and communicated with the right atrium through a patent foramen ovale about the size of the septal opening. The right ventricle was enlarged and hypertrophied. Microscopically, the septum consisted of elastic and collagenous tissue interspersed with scattered plain muscle fibres and a single layer of cardiac muscle in the outer half of the septum, but completely separated from the muscle in the auricular wall.

Eighteen cases previously reported are briefly reviewed. In most there was an incomplete septum or several foramina, and several patients lived to adult life. Death was usually from congestive heart failure. The mechanism of formation of the anomalous septum is discussed, and it is suggested that there is a defect at the junction between the pulmonary veins and the right auricle, due to a developmental arrest late in the second month of foetal life. *J. W. Litchfield*

1573. **Survival to the Age of Seventy-five Years with Congenital Pulmonary Stenosis and Patent Foramen Ovale**
P. D. WHITE, J. W. HURST, and R. H. FENNELL. *Circulation* [*Circulation*] **2**, 558–564, Oct., 1950. 3 figs., 35 refs.

HYPERTENSION

1574. **Treatment of Severe Hypertension with Hexamethonium Bromide**
A. CAMPBELL and E. ROBERTSON. *British Medical Journal* [*Brit. med. J.*] **2**, 804–806, Oct. 7, 1950. 11 refs.

Eight patients with either essential hypertension or Bright's disease were kept in bed for 2 weeks or longer without improvement before hexamethonium bromide was given. The dose was increased over 10 days from 0·25 g. twice a day to 0·5 g. 4 to 6 times daily before meals. In all cases there was a fall in blood pressure with relief of symptoms which included headache, paroxysmal nocturnal dyspnoea, and angina. Papilloedema regressed and vision improved. Postural hypotension caused transient symptoms and 2 patients had apparent paralytic ileus which responded to withdrawal of hexamonium for 24 hours and a high enema. Other transient side-effects were blurring of vision, dry mouth, nausea, heartburn, and constipation. Two out-patients have remained well without rise in blood pressure after stopping the drug. The remainder are well on a maintenance dose.

The good immediate results which were obtained prompted this preliminary report; the long-term value of the drug has yet to be assessed. [The conditions under which the blood pressures were recorded are not stated.] *D. Verel*

1575. **Effect of Dietary Restriction of Salt and Protein on Blood Pressure of Hypertensive Rats**
H. G. DANFORD, D. G. DIETER, J. W. CHRISTOFFERSON, and R. C. HERRIN. *American Journal of Physiology* [*Amer. J. Physiol.*] **163**, 190–196, Oct., 1950. 11 refs.

Hypertension was induced in 43 rats by wrapping the kidneys in silk. A control group of 15 were given normal diet and the remaining 28 rats were given various diets containing 0 to 0·5% of sodium chloride. Of the rats kept on a low-salt diet, 15 showed a fall in systolic pressure of 15 to 51 mm. Hg, diets with the lowest salt content having the greatest hypotensive effect. The time required to produce a significant fall in arterial pressure was 15 to 30 days. There was no significant loss in weight. Addition of 4 to 18% of casein to the diet did not affect the results. Only 40% of the control rats lived for 220 days after the operation, whereas 83% of the animals taking a low-salt diet survived this period. *A. Schweitzer*

1576. **A Hypertensive Syndrome with Relative Adrenal Cortical Overactivity**
D. F. DAVIES and H. E. CLARK. *Circulation* [*Circulation*] **2**, 494–504, Oct., 1950. 3 figs., 37 refs.

The authors studied adrenal cortical function (as reflected in the concentration of salt in the sweat) in two groups of patients with hypertension, one consisting of 16 women and 6 men with no clinical evidence of endocrine disorder, and the other of 24 women who were considered to have evidence of endocrine disorder in the form of a central obesity (which was often excessive and of sudden onset, sometimes associated with distur-

bances of menstruation), hirsutism, striae on the abdomen and thighs, and a tendency to bruise easily. In a few cases glycosuria or a diabetic type of glucose tolerance curve was found. A control group of 10 men and 11 women in normal health was also studied, as were 8 normotensive, obese women.

The subjects were placed in a steam room heated to 102° to 110° F. (38·9° to 43·3° C.) and at the end of 30 minutes samples of sweat were collected from their backs. The sweat from those patients judged to have the "endocrine hypertensive syndrome" contained a significantly lower salt concentration than that from the others; this is taken to indicate hyperactivity of the adrenal cortex. *H. E. Holling*

1577. **The Nature of Pressor Substances in Pheochromocytomas**

D. M. PITCAIRN and W. B. YOUMANS. *Circulation* [*Circulation*] **2**, 505–512, Oct., 1950. 5 figs., 31 refs.

A comparison of the effects of extracts of two pheochromocytomata on the arterial pressure of dogs showed that one tumour contained predominantly an adrenaline-like substance, while the principle in the other tumour resembled noradrenaline. "Dibenamine" was found to block the effect of adrenaline, but as with other such agents its effect in blocking the pressor action of noradrenaline was inconstant. A review of the evidence is presented which suggests that in the body noradrenaline is a precursor of adrenaline. *H. E. Holling*

1578. **Pressor Substances in Arterial Hypertension. II. Demonstration of Pherentasin, a Vasoactive Material Procured from Blood**

H. A. SCHROEDER and N. S. OLSEN. *Journal of Experimental Medicine* [*J. exp. Med.*] **92**, 545–559, Dec., 1950. 1 fig., 17 refs.

Pherentasin, a highly active pressor substance producing a prolonged effect in the rat, has been obtained in fairly pure form from the arterial blood of patients with hypertension. Its presence has been demonstrated by two biological methods. It was rarely found in normotensive blood. The blood of patients with renal or nephrogenic hypertension, either primary or secondary, consistently yielded this material. The blood of patients exhibiting neurogenic hypertension and the endocrine hypertensive syndrome had smaller amounts of it. Little or none was found in malignant hypertension. Perhaps pherentasin has a causal relation to the existence of arterial hypertension.—[Authors' summary.]

1579. **Pressor Substances in Arterial Hypertension. III. Chemical Studies on Pherentasin**

N. S. OLSEN and H. A. SCHROEDER. *Journal of Experimental Medicine* [*J. exp. Med.*] **92**, 561–570, Dec., 1950. 4 figs., 7 refs.

Pherentasin (see Abstract 1578) is of small molecular size, non-protein in nature, dialysable, soluble in water and 90% ethanol, and extractable into organic solvents from alkaline solution. It contains an amino group essential to activity, which is probably primary, and also contains an active carbonyl group. It has been found in concentrations up to approximately 20 γ per litre of blood.—[From the authors' summary.]

1580. **A Simple Mechanical Depressor Test in the Study of Changes in Blood Pressure.** (Una simple prueba mecanica depresora para el estudio de la variabilidad de la presion arterial)

D. GROSS. *Prensa Médica Argentina* [*Prensa méd. argent.*] **37**, 2580–2593, Oct. 27, 1950. 1 fig., 28 refs.

The author gives a general account of various pressor and depressor tests used in the study of blood-pressure changes. A new test is described, based on the reflex fall that occurs in arterial pressure following the momentary forcing of the point of a small ebonite pyramid into the skin of the arm by means of a sphygmomanometer cuff pumped up to a pressure of 200 mm. of mercury. In normal individuals there occurs an average fall of 12 mm. in the systolic and 5 mm. in the diastolic pressure. A greater fall is found in the early stages of essential hypertension, and the fall is less than normal in renal hypertension and advanced essential hypertension. *René Méndez*

1581. **Bilateral Adrenalectomy in Malignant Hypertension and Diabetes**

D. M. GREEN, J. N. NELSON, G. A. DODDS, and R. E. SMALLEY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 439–443, Oct. 7, 1950. 6 figs., 27 refs.

The authors discuss the role of the adrenal cortex in the production of essential hypertension and report briefly the results in 4 cases in which therapeutic unilateral adrenalectomy was carried out, in 3 of which glucose tolerance was impaired before operation. They draw no conclusions from these cases. A case is also reported in which diabetes mellitus and hypertension were present and in which bilateral adrenalectomy was performed, this case being described in detail. The patient was a housewife, aged 28, whose diabetes began at the age of 6 and who now needed 70 to 85 units of insulin a day. Hypertension had been noted at the age of 20, and she now had retinal haemorrhages and exudates and mild papilloedema. The blood pressure was 270/140 mm. Hg, the heart enlarged, and the electrocardiogram showed evidence of left heart strain. The adrenals were removed at two operations separated by 4 months, and her post-operative management with deoxycortone acetate (DCA) and cortical extract is well described, the results suggesting that aqueous cortical extracts contain a DCA-like substance capable of promoting hypertension. The treatment of hypertension by the operative production of Addison's disease seems worth considering in cases where the prognosis is otherwise hopeless. The patient's blood pressure 15 months after operation was 150/100 mm. Hg, her insulin requirements were 24 units a day, her renal function had improved, and the heart size and electrocardiogram were within normal limits. *G. S. Crockett*

Disorders of the Blood

1582. **The Effect of Transfusions and Antibiotics upon the Duration of Life in Children with Lymphogenous Leucemia**

H. R. Bierman, P. Cohen, J. N. McClelland, and M. B. Shimkin. *Journal of Pediatrics* [*J. Pediat.*] **37**, 455–462, Oct., 1950. 4 figs., 22 refs.

An analysis was made of the period of survival in relation to treatment in 76 (consecutive) cases of lymphatic leukaemia admitted to the paediatric department of the University of California Hospital during the period 1939–48. The average age of onset was 5 years, with a range of 3 months to 14 years, peaks of incidence occurring at 2 years and 4 years. Males predominated. In an attempt to ascertain how far treatment affected the duration of life the cases were divided into 4 groups: the first (18 cases) had had no treatment; the second (17) had been treated by irradiation and, at some time during the course of the illness, with blood transfusion and penicillin or sulphonamides; the third (24) had received blood transfusions, but no antibiotics; and the fourth (17) had been given blood transfusions, and penicillin and/or sulphonamides.

The average duration of survival was not significantly different in the first three groups, being 5·6 months, 5·8 months, and 6·0 months respectively. In the fourth group it was 8·9 months, the difference being statistically significant. The authors emphasize that as 17 to 25% of cases in the first three groups survived longer than 9 months, claims for therapeutic measures must be based not on individual cases, but on properly controlled series in which the influence of blood transfusions, antibiotics. and antihaemorrhagic agents is taken into account, This applies especially to the assessment of the therapeutic efficacy of the folic-acid antagonists and other new agents. *David Morris*

1583. **BCG Vaccination in Sarcoidosis**

H. L. Israel, M. Sones, S. C. Stein, and J. D. Aronson. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 408–417, Oct., 1950. 2 figs., 10 refs.

A study of B.C.G. vaccination under controlled conditions in 20 patients with sarcoidosis indicates that patients with this disease are unable to develop and maintain skin sensitivity to tuberculin. Atypical local reactions occur at the site of vaccination in a small number of patients with sarcoidosis, but, in the majority, the local reaction is indistinguishable from normal. Vaccination with B.C.G. does not provide significant assistance to the clinician as a diagnostic or therapeutic agent.

The failure of development of skin sensitivity to tuberculin in patients with sarcoidosis does not establish sarcoidosis as an anergic form of tuberculosis. The tuberculin anergy exhibited by patients with sarcoidosis appears to be nonspecific, due to interference with general immunologic mechanisms.—[Authors' summary.]

1584. **Sarcoidosis: a Survey, with Report of Thirty Cases**

B. Robinson and A. W. Pound. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 568–582, Oct. 14, 1950. 20 figs., 33 refs.

This Australian survey of sarcoidosis largely bears out the conclusions as to its aetiology and characteristic features which were arrived at by the Conference on Sarcoid of the National Research Council, Washington, in 1948. The history of the subject is briefly outlined, and the authors describe the very typical histological lesion with its characteristic granuloma going on to fibrosis. They state that " where any doubt has been raised in our minds as to the histological diagnosis of this ' sarcoid reaction ', the ultimate diagnosis has proved to be that of some other condition ". The lesion is not specific to this particular disease, non-caseating tubercles of this type also occurring in leprosy, brucellosis, beryllium poisoning, fungus infections, and certain other conditions. The non-caseating granuloma of tuberculosis can be distinguished only by finding tubercle bacilli.

The present series of patients was collected over a period of 3 years from many sources in Australia, 75 suspects being examined, of whom 30 proved to be cases of sarcoidosis. The features of these cases are described in some detail. The diagnostic criteria used were: (1) the presence of a group of signs suggestive of the disease; (2) the typical histological appearances of biopsy material; (3) the chronic and relatively asymptomatic course of the disease; (4) failure to demonstrate the tubercle baçillus by any method; (5) the absence of tuberculin sensitivity, which may change during the course of the disease. The age at which overt signs were first noted ranged from 17 to 60 years; in 17 cases the onset was between 25 and 35, in 6 between 50 and 60. The sexes were equally represented. The duration of the disease and of individual lesions varied greatly; in some cases it extended over 20 years, in others it cleared in a few months.

The organs most often involved were lungs, lymph nodes, skin, and eyes; these, however, are accessible organs and various others may be involved; in the one case coming to necropsy, much more extensive visceral involvement was found than had been suspected during life. Superficial lymph nodes were enlarged in 27 cases, and the mediastinal nodes in 18, in one of which there was no enlargement of superficial nodes. The skin was involved in 11 cases, always with other organs. Lungs were affected in 21 cases, and only one of these was discovered by routine *x*-ray examination. The upper respiratory tract showed lesions in 4 patients, the nose and accessory sinuses in 4, and the larynx in one. Eyes were involved in 6 cases, but no patient had a fully developed Heerfordt's syndrome. Bone was affected in only one patient in whom the lesion was associated with gross lupus pernio of the overlying skin. Hepatic

enlargement occurred in 11 cases; out of 3 liver biopsies positive results were found in 2. The spleen was enlarged in 6 patients, but never grossly. No significant anaemia was found; 2 patients had mild polycythaemia associated with extensive lung lesions. Monocytosis occurred in 13 cases and eosinophilia in 3 (in one of which it was due to hydatid cyst of the lung). The serum protein level was over 8 mg. per 100 ml. in 10 out of 27 cases examined, due in all except 2 to increased globulin content; the increase was always related to widespread disease. Tuberculin sensitivity was extensively tested; 3 patients were positive to 1 in 1,000 old tuberculin and one to 1 in 100; none was sensitive to avian tubercle bacilli. The Wassermann and Kahn reactions were always negative. Attempts to isolate tubercle bacilli from various sources, and virus from biopsy material, failed.

The forms of treatment tried included *x* rays and calciferol in doses of 30,000 to 100,000 units daily for some months; these had some, but variable, effect. Streptomycin, penicillin, arsenicals, bismuth, gold, and ultraviolet rays were all without effect. The disease is interpreted as a chronic infective process of unknown aetiology. *M. C. G. Israëls*

HAEMATOPOIETIC SYSTEM

1585. **Multiple Myeloma. Lesions of the Extra-osseous Hematopoietic System**
J. CHURG and A. J. GORDON. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 934–945, Oct., 1950. 13 figs., 25 refs.

The authors have reviewed the necropsy material from 30 cases of multiple myeloma encountered from 1933 to 1948 at the Mount Sinai Hospital, New York, and report on the incidence, character, and significance of the extra-osseous lesions found.

Extra-osseous myeloma cells were identified by their general morphology and by comparison with the cells in the marrow. In many cases a small myeloma cell was found, about half the size of a typical myeloma cell but with a similar "spoked-wheel" pattern. In 73% of cases, extraskeletal myeloma lesions were found in the spleen, liver, or lymph nodes, sometimes in all three. In the spleen the myeloma cells were seen first in the sinusoids and intersinusoidal cords, but when there was much infiltration the pattern became obscured. The organ was enlarged in about half the cases.

The retroperitoneal group of lymph nodes appeared to be the ones most commonly involved. They were discrete, and moderately enlarged and firm. In early cases microscopical examination revealed scattered myeloma cells, with later complete replacement of the normal lymphoid tissue.

In 14 cases the liver was infiltrated and either normal in size or moderately enlarged. Small white discrete nodules were found beneath the capsule or in the parenchyma; in some cases there was diffuse grey streaking. On microscopical examination myeloma cells were found in the sinusoids, either singly or in clumps. In more advanced cases large masses of cells were seen. Other organs were rarely involved and never without splenic, hepatic, or lymph-node involvement.

The authors point out that lesions are of three types: vascular, diffuse, and discrete. They agree that the origin of the myeloma cell is the primitive reticulum cell, and believe that their material did not suggest an endothelial origin. The small myeloma cells seen resembled both lymphocytes and the primitive marrow "small reticulum cell" of Rohr. They believe that a monophyletic small stem cell exists in the marrow and mesenchymal tissue, and may give rise to myeloma cells and plasma cells.

[Good photomicrographs accompany the paper.]
T. M. Pollock

1586. **Clinical and Pathologic Effects of Space-occupying Lesions of the Bone Marrow**
A. V. PISCIOTTA. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **20**, 915–933, Oct., 1950. 8 figs., 42 refs.

A leuco-erythroblastic blood picture consisting of a progressive anaemia, a low or occasionally elevated leucocyte count, and the presence of immature red and white cells in the peripheral blood may be associated with a wide variety of lesions of the bone marrow. This paper illustrates some of these lesions and describes the effects on the blood-forming organs.

Of the reported cases, 2 were of carcinoma and one was of multiple myeloma, one of lymphosarcoma, and one of malignant melanoma. There was one case of reticulo-endotheliosis with myelofibrosis, and 2 cases of myelofibrosis and osteosclerosis are included.

In the peripheral blood the erythrocyte count may at times be within normal limits. Immature myeloid or erythroid cells in the peripheral blood are, however, a constant feature and, as an indication that the bone marrow is being occupied by a progressive lesion, are of prognostic significance. The presence of immature blood cells was most pronounced in the cases of myelofibrosis. In one case haemolysis was noted.

As regards the concept of compensatory extramedullary haematopoiesis, it is pointed out that cases have been described in which visceral haematopoiesis did not result although the bone marrow was completely occupied by extraneous tissue; in one case of this series extensive visceral production of myeloid cells proceeded although the bone marrow was hyperplastic.

The diagnosis, and the part played in it by sternal and splenic puncture and lymph-node biopsy, are discussed.
T. M. Pollock

1587. **Effects of Nitrogen Mustard on the Bone Marrow in Polycythemia Vera**
C. C. SHULLENBERGER and C. H. WATKINS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 841–853, Oct., 1950. 3 figs., 10 refs.

In an attempt to determine how far nitrogen mustard acts selectively on erythropoietic tissue, and hence to assess its potential value in the treatment of polycythaemia vera, the authors carried out serial sternal-marrow

examinations in 6 cases under treatment with the drug at the Mayo Clinic. The following routine was adopted: the volume of packed erythrocytes was reduced to 50 to 60 ml. per 100 ml. of blood by repeated venesection; sternal aspiration was carried out immediately before starting treatment with nitrogen mustard in a total dosage of 0·4 mg. per kg. body weight given in 2 or 4 consecutive daily intravenous injections; subsequently, 1 to 4 sternal aspirations were performed at intervals varying from 24 to 120 hours after the first injection, and in one case again after 3 weeks and after 5 months. In 2 additional cases, marrow specimens were obtained only before treatment. The ratio of myeloid to erythroid cells was lower than normal in all pre-treatment specimens; by comparison, later specimens showed a reduction in the proportion of erythroid cells, although in 3 cases this was thought to be accompanied by general marrow hypoplasia. Morphological changes attributed to the action of nitrogen mustard are described. In 3 cases the condition relapsed between 3 and 5 months after treatment, and these patients received a second course of nitrogen mustard; 5 (and 3 others whose bone marrow was not examined and who were therefore omitted from the present report) remained in remission after periods of 2 to 14 months.

The authors conclude that, in spite of the evidence indicating that nitrogen mustard has a relatively greater action on erythropoiesis than on myelopoiesis, it has not yet been shown to be suitable for routine treatment of polycythaemia vera. *H. McC. Giles*

1588. **The Effect of Choline on Haematopoiesis.** (Azione della colina sulla ematopoiesi)
A. CANIGGIA. *Haematologica* [*Haematologica*] **34**, 625–638, 1950. 37 refs.

The effect of choline on the blood picture was studied in 12 patients—2 with pernicious anaemia, 2 with haemolytic jaundice, 1 with post-haemorrhagic anaemia, 1 with severe hypochromic anaemia of unknown origin, and 6 with post-infective anaemia. In all cases peripheral blood and bone-marrow smears were examined. Two patients were treated with choline chloride 1 g. a day for 12 to 20 days, 8 with 2 g. a day for 10 to 25 days, and 2 with 2 g. a day for 15 days plus 0·6 g. of iron a day as sulphate. In all cases the regimen of choline supplements produced marked changes in the blood and marrow. Erythrocytes increased in number, with a moderate reticulocytosis, diminution in mean corpuscular volume, restoration of haemoglobin content; there was also a diminution in the number of megaloblasts and accelerated maturation of erythroblasts. Moderate leucocytosis and a shift of Arneth's curve to the left were noted. The addition of iron increased the haemoglobin level and prevented the fall in mean corpuscular volume.

It is suggested that choline has a three-fold action: mobilizing and reducing hepatic fat; playing a part in the synthesis of methionine; and acting directly on the bone marrow as a stimulant to cellular proliferation. Choline should be included in anti-anaemic regimens. [There is no mention in this paper of control observations on similar patients.] *James D. P. Graham*

ANAEMIA

1589. **Colloidal Iron: a Well Tolerated, Effective Oral Hematinic**
A. J. CRESKOFF. *American Journal of Medical Sciences* [*Amer. J. med. Sci.*] **220**, 553–556, Nov., 1950. 4 refs.

Many people find iron in any form very unpleasant and even nauseating. Moreover, some of the commonly used tablets and syrups are not only unpleasant, but even dangerous if placed within access of children. Accordingly a search has long been made for a palatable and efficacious preparation of iron for use in the treatment of hypochromic microcytic anaemia. Satisfactory results are reported with a colloidal form of iron in casein digested with papain. [The preparation advised in this communication is not entirely new, but it seems to have appealed to the author very much and he reports upon his short list of cases with naïve enthusiasm.]
G. F. Walker

1590. **Production of Specific Antisera against Sickle Cell Anemia Erythrocytes; Antibody in Sicklemia Sera**
R. G. SCHNEIDER and W. C. LEVIN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 110–114, Oct., 1950. 4 refs.

HAEMOLYTIC ANAEMIA

1591. **Erythroblastosis Fetalis. III. Prognosis in Relation to Clinical and Serologic Manifestations at Birth**
L. K. DIAMOND, V. C. VAUGHAN, and F. H. ALLEN. *Pediatrics* [*Pediatrics*] **6**, 630–637, Oct., 1950. 5 refs.

In a series of 224 Rh-positive infants of sensitized Rh-negative mothers observed at the Children's and Lying-in Hospitals, Boston, Massachusetts, an attempt was made to correlate certain clinical and serological findings at birth with the incidence and severity of erythroblastosis foetalis and kernicterus.

Yellow vernix or discoloration of the umbilical cord may be present when the baby is born but, despite careful inspection, the authors have never seen bile-staining of the skin or sclera at the moment of birth. This may make its appearance after an interval ranging from an hour to a day or more, but must be very exceptional at birth. Neither the rapidity with which jaundice develops nor its intensity is of prognostic significance, but in those cases in which the jaundice begins to fade by the third to fifth day of life recovery will usually be complete. Amongst babies surviving for more than a week, those developing kernicterus always have marked jaundice, which persists longer than in those without subsequent kernicterus. In general the more severe the anaemia and the splenic enlargement at the time of birth, the more unfavourable is the outlook, but the mortality is not related to the incidence of kernicterus. While babies with an erythrocyte count of less than 3,000,000 per c.mm. are undoubtedly more likely to die than those with a higher count, the incidence of kernicterus is virtually independent of the degree of anaemia.

With regard to serological findings there is no evidence

relating the severity of the illness to the presence of "blocking" activity in the infant's erythrocytes. Similarly the result of the Coombs test is without value for the prognosis in erythroblastosis foetalis. The authors have seen many babies with a strongly positive reaction to Coombs's test who had no clinical sign of erythroblastosis, while a negative reaction has been found in a few fatal cases. Unfavourable results (chiefly kernicterus) tend to be more frequent in cases where the ratio of antibody titre of the maternal blood to that of the infant's blood is high (16 to 1 or greater), suggesting a greater affinity of the child's erythrocytes for antibody.

While there was no significant sex difference in the incidence of erythroblastosis in this series, the disease did appear to take a more severe form in the males, the reasons for which were not clear. Why the severity of kernicterus bears no relation to that of the other clinical signs of erythroblastosis foetalis has yet to be elucidated. Those deaths that are not associated with kernicterus occur predominantly on the first day of life, whereas death from kernicterus occurs later in the first week of life. It is suggested that the latter is due to a different pathological mechanism from that which leads to early death in babies with severe anaemia and marked hepatosplenomegaly.

Jas. M. Smellie

1592. **Erythroblastosis Fetalis. VI. Prevention of Kernicterus**

F. H. ALLEN, L. K. DIAMOND, and V. C. VAUGHAN. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 779–791, Nov., 1950. 2 refs.

The incidence of kernicterus and its relation to treatment and other factors were studied in a series of 368 liveborn Rh-positive babies of sensitized Rh-negative mothers observed over a 5-year period at the Children's Medical Center and the Lying-in Hospital, Boston, Massachusetts. Immature babies developed kernicterus more frequently than mature babies, and there was a significant reduction in the incidence of kernicterus among those babies, whether immature or mature, who were treated by exchange transfusion. There was a constant close relationship between the depth of jaundice and the occurrence of kernicterus, and an increased tendency to kernicterus when the maternal antibody titre was high. However, exchange transfusion lowered the incidence of kernicterus even when the maternal antibody titre was high, so that in these patients the relation of titre to kernicterus was no longer significant.

The authors conclude that prematurity, being associated with a high incidence of severe jaundice, results in an increased tendency to kernicterus, and consider that early induction of labour should be rigidly avoided in cases of Rh-sensitization. The adoption of a deliberate policy of not inducing labour before the 38th week did not result in an increased number of stillbirths or hydropic infants. Male babies were found to be more prone to develop kernicterus, 17·8% of 269 males, and 8·9% of 246 females, developing this complication. The authors consider that for exchange transfusion blood from a female donor is to be preferred [but other workers (Sacks *et al.*, *Pediatrics*, 1950, **6**, 772) do not agree with this conclusion]. A scheme of treatment for infants with erythroblastosis foetalis based on the above observations has been introduced, and only 1 out of 109 infants so treated has developed kernicterus.

Three problems remain unexplained: (1) why kernicterus is not seen in stillborn babies or in babies dying before about 24 hours of age, many of whom have considerably elevated serum bilirubin levels; (2) why kernicterus does not occur after the first 5 days of life, even in immature infants in whom the serum bilirubin level remains high for a month or more; and (3) why certain babies (perhaps 30 to 35%) are apparently not susceptible to kernicterus in any circumstances.

R. M. Todd

1593 (*a*). **Erythrocyte Survival Studies in Childhood. I. Methods and General Observations**

E. KAPLAN and W. W. ZUELZER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 511–516, Oct., 1950. 4 figs., 7 refs.

In this series of reports on a long-range study of the anaemias of infancy and childhood, the authors describe the results of approximately 100 erythrocyte-survival experiments. Blood was taken from both healthy donors and patients with haematological disorders, stored at 4° C., and transfused usually within 24 hours of withdrawal. The usual amount of transfusion was 4 to 9 ml. of citrated whole blood per lb. (8·84 to 19·9 ml. per kg.) body weight. The survival of transfused erythrocytes was determined by the differential haemagglutination technique. Post-transfusion erythrocyte counts, performed at daily intervals for several days and then at 7- to 10-day intervals, were expressed as percentages of the initial post-transfusion count, which was at least 200,000 cells per c.mm.

Erythrocytes from normal donors transfused into normal infants gave a roughly linear survival curve, having a half-life of 46 to 80 days and a maximum life of 100 to 120 days. Normal survival curves were obtained when normal erythrocytes were transfused into children with sickle-cell anaemia, congenital haemolytic icterus, and Mediterranean anaemia. A rapid elimination of donor cells was observed when erythrocytes from patients with sickle-cell anaemia (including one who had had a splenectomy 6 years previously) and congenital haemolytic icterus were transfused into normal individuals, indicating the presence of an intracorpuscular defect. These results confirm those of previous workers.

Harold Caplan

1593 (*b*). **Erythrocyte Survival Studies in Childhood. II. Studies in Mediterranean Anemia**

E. KAPLAN and W. W. ZUELZER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 517–523, Oct., 1950. 4 figs., 7 refs.

Erythrocytes from 3 children with typical Mediterranean anaemia were transfused into normal recipients. There were accelerated elimination of 25 to 50% of the cells, and normal survival of the remainder. The survival time of erythrocytes from 3 carriers of Mediterranean anaemia (mothers of children with the disease)

and from a child with gross iron-deficiency anaemia was normal when transfused into normal recipients. Normal erythrocytes survived normally when injected into patients with Mediterranean anaemia.

These findings indicate the presence in Mediterranean anaemia of a haemolytic mechanism due to an intracorpuscular erythrocyte defect which is not apparent in the carrier state, and which is not simply related to a quantitative deficit in erythrocyte haemoglobin. It is suggested that in this disease those erythrocytes in which the basic defect in structure or composition is associated with marked deformities of shape are destroyed rapidly while the remainder survive normally.

Harold Caplan

1593 (*c*). **Erythrocyte Survival Studies in Childhood. III. Unusual Familial Hemolytic Anemias associated with Intrinsic Erythrocyte Abnormality**

E. KAPLAN and W. W. ZUELZER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 524–530, Oct., 1950. 3 figs., 7 refs.

The blood of 3 siblings of 2 families with atypical chronic familial haemolytic anaemias was investigated. There were no characteristic morphological or other abnormalities of the erythrocytes *in vitro*. Erythrocytes from one of these children were rapidly eliminated after their transfusion into a normal recipient, whereas erythrocytes from a normal donor transfused into the affected children survived normally, suggesting an intracorpuscular defect as the basis for the haemolytic mechanism. One of these children, however, was later admitted with the appearance of a fulminating haemolytic crisis with massive haemaglobinuria, and atypical auto- and iso-agglutinins were demonstrated in the patient's serum. The erythrocyte survival curve after transfusion of normal blood 5 days after the onset of the crisis was now characterized by the rapid elimination of 60% of the transfused cells, followed by a very slow elimination of the remainder, thus demonstrating a superimposed acquired extracorpuscular haemolytic disturbance.

Harold Caplan

PERNICIOUS ANAEMIA

1594 (*a*). **Absorption of Vitamin B_{12} in Pernicious Anaemia. I. Oral Administration without a Source of Intrinsic Factor**

C. C. UNGLEY. *British Medical Journal* [*Brit. med. J.*] **2**, 905–908, Oct. 21, 1950. 2 figs.

The experiments described in this and the succeeding three papers were designed (*a*) to determine how effectively vitamin B_{12} is absorbed when given alone or with gastric juice, and (*b*) to determine whether Castle's intrinsic factor directly facilitates the absorption of vitamin B_{12} or merely protects it from destruction in the gastrointestinal tract.

This first paper deals with the oral administration of vitamin B_{12} alone to patients suffering from pernicious anaemia in the stage of relapse. In each case the effective oral dose was compared with the parenteral dose expected to produce a similar increase in erythrocyte count in 15 days. In one patient daily doses of 5 μg. were ineffective during a period of 10 days. In another patient 80 μg. daily for 24 days produced an increase in erythrocyte count no greater than would have been expected in 15 days after a single parenteral injection of 2·5 μg. Five other patients received single oral doses of 3,000 μg. The reticulocyte response was maximal in all, and the erythrocyte-count increase during 15 days equivalent to what would be expected from a single injection of 80 to 160 μg. "These findings suggest that some vitamin B_{12} can be absorbed—not efficiently perhaps, but in quite considerable amounts if the dose is large enough—without first combining with intrinsic factor."

L. J. Davis

1594 (*b*). **Absorption of Vitamin B_{12} in Pernicious Anaemia. II. Oral Administration with Normal Gastric Juice**

C. C. UNGLEY. *British Medical Journal* [*Brit. med. J.*] **2**, 908–911, Oct. 21, 1950. 2 figs.

Varying quantities of vitamin B_{12} were added to varying quantities of pooled normal gastric juice, which had previously been neutralized to *p*H 7 with N/1 sodium hydroxide, and given by mouth to patients with pernicious anaemia within either 2 or 6 hours of being mixed, food being withheld for 4 hours before and after. Dosage ranged from 5 μg. vitamin B_{12} in 50 ml. gastric juice given daily for 10 or 15 days, to 80 μg. vitamin B_{12} in 500 ml. gastric juice given in a single dose. In all, 8 patients were studied. It was shown in one experiment that the passage of the gastric juice through a Seitz filter rendered it ineffective, since the daily administration of 5 μg. vitamin B_{12} in 50 ml. of such filtered gastric juice evoked no response, although when unfiltered gastric juice was substituted, an optimal response resulted. Considering the results as a whole it appears that they were very variable. In 4 of the patients the effect of vitamin B_{12} given orally with gastric juice was about as effective as if the same dose had been injected parenterally. In 2 it was concluded that only about 10% of the vitamin was absorbed, in another case no response followed the administration of 50 μg. vitamin B_{12} in 500 ml. gastric juice, while in the last case the response was very poor to 40 μg. in 150 ml. gastric juice. It is concluded that the amount of gastric juice necessary to promote absorption of a given amount of vitamin B_{12} varies considerably; each 100 ml. of gastric juice seemed enough for 10 μg. of vitamin B_{12} in 4 cases, while in the other cases the figure ranged from 0 to 5 μg.

L. J. Davis

1594 (*c*). **Absorption of Vitamin B_{12} in Pernicious Anaemia. III. Failure of Fresh Milk or Concentrated Whey to Function as Castle's Intrinsic Factor or to Potentiate the Action of Orally Administered Vitamin B_{12}**

C. C. UNGLEY. *British Medical Journal* [*Brit. med. J.*] **2**, 911–915, Oct. 21, 1950. 5 figs.

The possibility that milk might have similar properties to gastric juice in potentiating the action of vitamin B_{12} when administered orally was explored in clinical trials

on 5 patients suffering from pernicious anaemia in relapse. Two of them received 500 ml. of fresh milk plus 10 μg. of vitamin B_{12} daily, while the others were given whey derived from 7 litres, 3 litres, and 6 litres of milk respectively, to which 50 μg. of vitamin B_{12} had previously been added. The whey mixture was given by stomach tube in a single dose to 2 patients, and in divided doses on consecutive days to the third patient. In no case was a significant haematological response obtained, although all the patients subsequently responded satisfactorily to the administration of folic acid, parenteral vitamin B_{12}, or oral vitamin B_{12} plus gastric juice.

L. J. Davis

1594 (*d*). **Absorption of Vitamin B_{12} in Pernicious Anaemia. IV. Administration into Buccal Cavity, into Washed Segment of Intestine, or after Partial Sterilization of Bowel**

C. C. UNGLEY. *British Medical Journal* [*Brit. med. J.*] **2**, 915–919, Oct. 21, 1950. 4 figs., 21 refs.

The object of the experiments described in this paper was to determine whether vitamin B_{12}, even without intrinsic factor, would be efficiently absorbed if destruction by intestinal contents could be avoided or could be reduced.

This was attempted in 3 ways: (1) Vitamin B_{12} was applied daily to the mucosa of the floor of the mouth between the alveolar margin and the cheek, a solution containing 5·5 μg. being added gradually to a pledget of cotton wool over a period of 30 minutes and water alone added for the next 30 minutes. Subsequent microbiological assay of 10 pledgets yielded 8 μg. of vitamin B_{12}. One patient tested in this way for 10 days showed no significant response, although he responded subsequently to 5 μg. of vitamin B_{12} plus 50 ml. of gastric juice given orally for 10 days. (2) Vitamin B_{12} was instilled into a segment of small intestine lying between 2 balloons attached to a Miller–Abbott tube, the isolated segment being previously washed with saline. This experiment was performed on 2 patients, the doses of vitamin B_{12} being 40 μg. and 80 μg. respectively, in 10 ml. water. Neither patient showed a significant response. In both patients the experiments were repeated, gastric juice being added to the vitamin B_{12} in one case, but the results were again negative. They both responded, however, to the subsequent administration of vitamin B_{12} by injection or with gastric juice by mouth. It is concluded, however, that little reliance can be placed on these negative results since the segment of intestine may have been too small, or unsuitably sited for absorption of vitamin B_{12}. (3) Preliminary treatment with phthalylsulphathiazole, aureomycin, and dihydrostreptomycin was given to a single patient with the object of destroying intestinal bacteria which might take up the vitamin. It was ascertained bacteriologically that after 5 days *Bacterium coli* and enterococci had disappeared from the stools and 80 μg. of vitamin B_{12} was then given orally, but without effect. The same dose was subsequently given orally together with 500 ml. of gastric juice, with only a slight response, but a more satisfactory result followed parenteral injection.

It is considered that the negative findings in these experiments do not support, but do not entirely exclude, the possibility that Castle's intrinsic factor acts by protecting vitamin B_{12} from destruction in the gastrointestinal tract.

L. J. Davis

1595. **Gastric Biopsy in Pernicious Anaemia**

R. K. DOIG and I. J. WOOD. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 565–568, Oct. 14, 1950. 6 figs., 24 refs.

The authors have developed a technique for blind gastric biopsy by means of a flexible tube, the details of which have been reported previously (Doig *et al*, *Lancet*, 1950, **1**, 948). The fragments obtained are about 1 mm. in diameter and are treated by the usual histological methods, with a special stain for pepsin granules. Haematemesis or melaena has occurred in only 5 out of 484 cases in which biopsy has been performed, and has never been serious. The gastric mucosa in 33 cases of pernicious anaemia appeared atrophic; it was less than half the average depth, there was almost complete atrophy of the gastric glands of the body, and pepsinogen granules were rare and few. The surface epithelium usually showed intestinal metaplasia with numerous goblet cells; sometimes islets of normal mucosa remained. Infiltration of the lamina propria, chiefly with lymphocytes, was present but was never dense. This contrasts with the findings in chronic atrophic gastritis, in which cellular infiltration was dense and polymorphs, plasma cells, and macrophages were present as well as lymphocytes; intestinal metaplasia was not common and residual clumps of chief and parietal cells were present. In specimens of gastric mucosa from cases of pernicious anaemia the authors have had no difficulty in demonstrating argentaffin cells, although it has been suggested by Jacobson that their absence is a feature of pernicious anaemia. Paneth cells, characteristic of intestinal epithelium, were observed in areas of intestinal metaplasia.

Biopsies were carried out in cases of pernicious anaemia before liver treatment, a few days after treatment was begun, and after some months of treatment, and in others after 1 to 25 years of adequate control. The appearances of the gastric mucosa were the same at all times; even after 25 years there was no evidence of regeneration. This finding differs from that reported by some gastroscopists.

The authors point out that many patients with anaemia are referred for diagnosis after ineffective attempts at liver treatment have been made, or when the original diagnosis was based on inadequate blood examination. The diagnosis is then very difficult, but gastric biopsy could provide a useful clue. Out of 46 patients with pernicious anaemia and subacute combined degeneration of the spinal cord, the appearance on biopsy was completely typical in all but 3; they also found 2 patients with typical gastric atrophy who had no sign of pernicious anaemia or subacute combined degeneration. Some useful photomicrographs are reproduced.

M. C. G. Israëls

Respiratory Disorders

1596. **Spirometry as a Means for Studying Ventilatory Function of Patients in Mechanical Respirators**
C. G. GRULEE, F. L. ELDRIGE, and G. D. FORD. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 511–521, Nov., 1950. 5 figs., 28 refs.

In the management of patients immured in any of the respiratory machines which are loosely called " iron lungs " the machinery should not be turned on and off in accordance with mere clinical judgment, valuable indeed as this may be. So far as possible, in every case where artificial respiration is being applied by mechanical means, spirometric observations should be made upon the patient so that his power of respiratory movement can be assessed and changes noted for better or worse. [Unfortunately most spirometric procedures do not take into account the changes due to anoxia brought about by alveolar failure. They merely record, and not very accurately, the changes due to the impairment of the powers of the intercostal muscles and the auxiliary muscles of respiration.] *G. F. Walker*

1597. **The Prophylaxis and Treatment of Acute Respiratory Diseases with Antihistaminic Drugs. I. Prophylactic Treatment in Navy Male Recruits. II. Prophylactic Treatment with Therapeutic Dosage in Navy Male Recruits. III. Treatment of Minor Acute Respiratory Infection in Navy WAVE Recruits**
UNITED STATES NAVAL MEDICAL RESEARCH UNIT NO. 4. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 555–583, Oct., 1950. 6 figs., bibliography.

An attempt was made to determine the effect of prophylactic administration of an antihistaminic drug (" thonzylamine hydrochloride ") upon the incidence of acute minor respiratory diseases among U.S. naval personnel. The dose given was 100 mg. daily. Great care was taken to minimize error and to ensure uniformity of classification of the various types of respiratory disease by examining physicians. Thus whereas the subjects appeared to be divided into a " treated " and an " untreated " group, in reality one-half of the " treated " group were given a placebo so that only one-third of those observed were given the drug, their identity being concealed from the observers. Administration of treatment was supervised and the assessment of its effect not dependent alone upon the patient's estimate. The occurrence of an influenza epidemic somewhat complicated the investigation, but the findings were clear enough to show that the drug had no effect upon the incidence or course of the common acute respiratory diseases.

A second study was undertaken after the influenza epidemic was over to determine whether the prophylactic administration of antihistaminic drugs in doses within the therapeutic range had any deterrent effect upon development of the common cold. Thonzylamine hydrochloride was given in a daily dosage of 225 mg. to one group, and " trimeton " (90 mg. daily) to another, while a third group received the placebo. There was no evidence that either drug prevented the development of colds or had any effect on their symptomatology or duration.

Finally, the therapeutic effect of thonzylamine in minor acute respiratory disorders was studied and compared with that of atropine and a placebo in 159 women auxiliaries of the U.S. Navy. The three groups showed no appreciable difference in respect of the symptomatology or duration of respiratory diseases occurring during the 14 weeks of the trial. An atropine-like effect of the antihistaminic was observed on the nasal mucosa, but this could not be regarded as a " cure " in view of the continuance of other characteristic signs and symptoms.
Richard D. Tonkin

1598. **Pulmonary Insufficiency. IV. A Study of 16 Cases of Large Pulmonary Air Cysts or Bullae**
E. DEF. BALDWIN, K. A. HARDEN, D. G. GREENE, A. COURNAND, and D. W. RICHARDS. *Medicine* [*Medicine, Baltimore*] **29**, 169–194, Sept., 1950. 8 figs., 13 refs.

At the Presbyterian and Bellevue Hospitals, New York, the authors observed the physiological pattern of pulmonary function in 16 patients with large air cysts or bullae and on the findings divided them into three groups: Group (1) (3 cases) had cysts communicating freely with the bronchial tree and associated with apparently normal remaining lung. The main disturbance was over-ventilation of areas poorly perfused with blood, resulting in an insufficient rate of gaseous exchange. After pneumonectomy in one case a 10% improvement in the breathing capacity and a return of the rate of oxygen removal to normal was observed. Group (2) (3 cases) had cysts with poor or intermittent bronchial communication and with apparently normal remaining lung. The total lung volume and maximum breathing capacity were greatly reduced. There was moderate hyperventilation, particularly on exercise, and the arterial blood oxygen saturation and carbon dioxide tension were normal. Hence the badly ventilated cysts were poorly perfused with blood and they interfered mechanically with the bellows action of the chest. After lobectomy in one case and pneumonectomy in another an increase in the lung volume (57% and 47% respectively) and in the maximum breathing capacity (52% and 138%) occurred. The ventilation and breathing reserve during standard exercise became normal. The results suggest that the extreme ventilatory deficiency was in part due to reflex bronchospasm caused by mediastinal displacement due to the cysts. Group (3) contained cases of cysts with poor or intermittent bronchial communication associated with chronic diffuse emphysema and is further divided into two sub-groups.

In sub-group (3A) (4 cases) the disability was found due to ventilatory insufficiency. Total lung volume was reduced and residual air increased. Maximum breathing capacity was severely diminished, but improved with a bronchodilator drug. Hyperventilation occurred during standard exercise, and the oxygen consumption, the rate of oxygen removal, and the gas content of arterial blood were normal. The one patient subjected to surgery was greatly improved. In sub-group (3B) (6 cases) findings were similar, except that there was in addition alveolar respiratory insufficiency, with arterial anoxia after exercise.

In cases of the type of group (1), surgical resection would be beneficial where there is disturbance of function; in those of group (2) it is necessary wherever possible; some cases of the type of group (3A) may benefit from surgery, but attempts at operation in cases of group (3B) have thus far led to post-operative death.

A. G. Beckett

1599. **Atelectasis and Bronchiectasis in Pertussis**
A. W. LEES. *British Medical Journal* [*Brit. med. J.*] **2**, 1138–1141, Nov. 18, 1950. 35 refs.

The author examined, clinically and radiologically, 150 consecutive cases of pertussis admitted to Ruchill Hospital, Glasgow, in 1946–7, with special reference to evidence of atelectasis and bronchiectasis. Weekly radiographs were taken when atelectasis was discovered, including lordotic and lateral views. In cases of collapse of marked or moderate extent, and in those of slight but persistent collapse, bronchoscopy was carried out if the child was over one year. A Mantoux test was performed in all cases on admission and again 8 weeks later. Collapse of the middle lobe and collapse complicated by infection and appearing as pneumonia are difficult to detect. For this reason doubtful small areas of collapse were not recorded as such unless confirmed by a radiologist. Radiological evidence of collapse was seen in 65 cases (43%), in some of which more than one lobe was involved. The left upper and right upper lobes were affected only 3 times in all, which is in sharp contradistinction to the incidence in tuberculosis. In 70% the atelectasis was classed as slight, in 18% moderate, and in 12% severe (with almost complete lobar collapse). It occurred mostly in the first 4 weeks of illness and seldom lasted longer than 5 weeks. Bronchopneumonia occurred in 30 of the 150 cases, but had no special influence on the incidence of collapse. Enlargement of the hilar glands was demonstrable in only 28 cases, and no instance of collapse could be attributed to this.

Bronchial dilatation in the collapsed area was found on bronchoscopy in 4 cases of marked collapse, but cleared up after re-expansion in 3 of these. In the fourth case, after 3 years, there was a suspicion of residual cylindrical dilatation both on radiological and clinical grounds. Of 10 cases of moderate collapse in which bronchography was performed 4 showed bronchial dilatation of slight extent which cleared subsequently. Where there was no evidence of collapse, bronchial dilatation was never demonstrated. Reversible bronchial dilatation therefore appeared to be the rule. Treatment was chiefly by postural drainage and percussion of the affected area, but in 4 cases of marked bronchial dilatation artificial pneumothorax was induced in order to take the strain off the bronchi; although these patients did well, no inference should be drawn from that fact.

The main difference between this series and others previously reported is that enlarged hilar nodes played no part in the production of atelectasis and that the lower lobes were the most commonly affected The lobar incidence of bronchiectasis in adults is very similar. The comparative frequency of reversible bronchiectasis is also noteworthy, although there is no doubt that mechanical dilatation caused by collapse may be rendered permanent if infection supervenes. Where the area of collapse is small the compensatory emphysema surrounding it is enough to take the strain off the bronchi. The author emphasizes that recurrent attacks of cough and pneumonia with persistent crepitations following pertussis call for bronchoscopy and treatment without delay. Re-expansion has been known to occur as long as 6 months after the onset of atelectasis, and surgical removal of the lobe in any case of less than one year's duration seems inadvisable. However, when pronounced bronchial dilatation is accompanied by obvious infection surgical treatment is indicated and chemotherapy and antibiotics are of value only in acute exacerbations.

Ronald S. McNeill

1600. **Pulmonary Cavitation due to Polyarteritis**
B. P. SANDLER, J. H. MATTHEWS, and S. BORNSTEIN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 754–757. Oct. 28, 1950. 7 figs., 6 refs.

The case is described in detail of a white male who complained of joint pains, fatigue, cough, dyspnoea, and weakness. On admission to hospital a radiograph showed a cavity in the right lung and a nodule at the left apex. He subsequently developed haematuria, testicular pain, pain in the legs, anaemia, haemoptysis, renal impairment, and skin lesions on the legs. Histological examination of necropsy material showed periarteritis nodosa causing large cavitations in the lungs; there was also involvement of the skin and internal organs. A review of the literature revealed no previous case of polyarteritis nodosa with radiological evidence of pulmonary cavitation. *Geoffrey McComas*

1601. **Pleural Effusions and Intrapleural Pressures of the Re-expansion Period in Pneumothorax**
T. G. HEATON. *Diseases of the Chest* [*Dis. Chest*] **18**, 324–329, Oct., 1950.

As a result of a study of intrapleural pressures during re-expansion after artificial-pneumothorax therapy, it is suggested that when the mean negative intrapleural pressure is more than −15 cm. of water, the formation of fluid is likely. The chief cause of effusion is stated to be trauma to thickened pleura incidental to pneumothorax treatment, and the recommendation is made that gradual re-expansion is preferable, except perhaps in cases where the visceral pleura is thin and the lung has previously shown a tendency to re-expand.

Kenneth Marsh

Digestive Disorders

STOMACH AND INTESTINES

1602. **The Effect of Sympathectomy on the Clinical Course of Peptic Ulcer**
N. C. HIGHTOWER, C. G. MORLOCK, and W. M. CRAIG. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **25**, 634–638, Nov. 8, 1950. 9 refs.

In view of the discrepancies of opinion on this subject in the literature the authors addressed themselves to the problem of determining the effect of sympathectomy, if any, on the development or course of peptic ulceration by studying the records of 963 patients who had been subjected to sympathectomy for hypertension at the Mayo Clinic between 1935 and 1949. Only 7 patients developed a peptic ulcer after the sympathectomy, while out of a further 14 patients who had pre-existing ulcer symptoms 8 were unchanged, 3 were better, and 3 were worse. They thus found no evidence that sympathectomy, as performed for hypertension, has any effect on the incidence or course of peptic ulceration. They enter the reservation that thoraco-lumbar and subdiaphragmatic sympathectomy, as carried out for the relief of hypertension, does not completely destroy the sympathetic supply to the gastro-intestinal tract.

Hermon Taylor

1603. **Gastric Analysis—Practical or Useless?**
R. RICKETTS. *Review of Gastroenterology* [*Rev. Gastroent.*] **17**, 893–915, Oct., 1950. 15 refs.

The arguments for and against routine gastric analysis are surveyed. The author insists that if the analysis is to be made at all it should be as full as possible. He gives a bread-and-water test meal and extracts fractions every 30 minutes until the stomach is empty. Samples are subjected to careful naked-eye and microscopical examination, as well as to the usual chemical analyses. From a series of 100 cases of gastro-duodenal lesions, illustrative case records and gastric analyses are selected for discussion. The final conclusion is that if the stomach can be studied gastroscopically and radiologically, gastric analysis is usually a redundant investigation. The special information provided by gastric analyses may, however, be required in certain circumstances, particularly as a contribution to knowledge of gastric physiology and pathology. *John Naish*

1604. **Non-specific Gastric Granulomata.** (Granulomas gástricos inespecíficos)
V. ARTIGAS, J. RUBIO, and P. ANFRES. *Revista Española de las Enfermedades del Aparato Digestivo y de la Nutrición* [*Rev. esp. Enferm. Apar. dig.*] **9**, 537–553, Sept.–Oct., 1950. 9 figs.

The authors give details of 3 cases of gastric tumours which, after operation and histological examination, were found to be non-specific granulomata. It is almost impossible to differentiate such cases clinically and radiologically from gastric neoplasms. Histologically, a very small proportion of gastric tumours can be classified as non-specific inflammatory granulomata. If on exploration a large gastric tumour with obvious adenopathy but no metastases is found, then it must be resected, for whereas this procedure may be only palliative in cases of carcinoma, it may well be curative if the lesion is granulomatous. Patients in this group are often poor operative risks and require special care before and after operation.

René Méndez

1605. **Effect of Beta Irradiation on Gastric Acidity**
R. F. HEDIN, W. R. MILLER, and D. G. JELATIS. *Archives of Surgery* [*Arch. Surg., Chicago*] **61**, 748–757, Oct., 1950. 11 figs., 14 refs.

By filling an intragastric balloon with a solution containing radioactive phosphorus the authors were able to destroy the gastric mucosa of dogs and cause them to become achlorhydric. Further studies are in progress to determine whether the method might be applied to the treatment of peptic ulcer.

[It will be interesting to know whether survivors develop pernicious anaemia.] *H. Daintree Johnson*

1606. **Question of the Return of Gastric Secretion after Complete Vagotomy**
L. R. DRAGSTEDT, E. R. WOODWARD, and E. H. CAMP. *Archives of Surgery* [*Arch. Surg., Chicago*] **61**, 775–786, Oct., 1950. 1 fig., 6 refs.

Experimental and clinical evidence is presented to show that divided vagus nerves do not regenerate.

Four dogs, whose stomach was isolated from the rest of the alimentary canal, but with nerve supply intact, survived 4 to 6 months after subsequent vagotomy, without any recovery of the greatly diminished secretion of hydrochloric acid. One similar dog survived 2 years. After vagotomy, acid secretion was reduced from 44·1 to 8·3 milliequivalents in 24 hours. At 2 years the figure was 11·3. In this animal the nerves had been crushed but not divided. In 6 other dogs with simple fistulae the nerves were crushed only. Insulin responses were still negative when the latest tests were made 3, 3, 2, and 2 years, and 9 and 4 months, after the event.

Of 19 patients whose vagi had been resected up to 7 years previously, 3, none of whom were tested directly after operation, now had positive insulin responses. In these 3 operation had reduced by 80% the average amount of hydrochloric acid secreted in 24 hours. One, 2, and 5 years later the average was still 60% below the preoperative level. In 3 cases insulin tests were not repeated. The remaining 13 were all insulin-negative and continued to show marked depression of acid secretion; though only 3 had had no free hydrochloric acid soon after operation, 7 were now achlorhydric.

Vanzant is said to have reported different results, but it is pointed out that she measured only acid levels and ignored volumes secreted.

[A later publication of Vanzant's (*Gastroenterol.*, 1947, **8**, 768) than the one referred to here mentions very little evidence of return of acidity in Hartzell's dogs after 2 years, though she has been repeatedly misquoted as having shown the effects of vagotomy to be temporary. Perhaps this is because of the wording of her summary.]

H. Daintree Johnson

1607. **ACTH and Gastrointestinal Enzymes**
S. J. GRAY, H. M. SPIRO, and R. W. REIFENSTEIN. *Bulletin of the New England Medical Center* [*Bull. New Engl. med. Center*] **12**, 169–176, Oct., 1950. 1 fig., 5 refs.

1608. **Gastric Ulcer in Childhood**
M. D. INGRAM. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 765–768, Nov., 1950. 11 refs.

See also Sections Genetics, Abstract 1361; Pharmacology and Therapeutics, Abstract 1397; Disorders of the Blood, Abstract 1595.

1609. **Effects of Chemotherapeutic Agents on Fecal Bacteria in Patients with Chronic Ulcerative Colitis**
H. C. MARSHALL, W. L. PALMER, and J. B. KIRSNER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 900–903, Nov. 11, 1950. 8 figs., 9 refs.

As reported elsewhere, administration of sulfonamides reduces the number of aerobic bacteria in the feces of previously untreated patients with chronic ulcerative colitis and appreciably alters the type of predominant organism. These changes may persist for as long as 6 weeks. After 6 weeks, or in patients who have previously received long-term treatment with sulfonamides, the bacterial flora resembles that of the untreated patient in type and quantity. The number of bacteria growing under anaerobic conditions is not markedly altered by the use of sulfonamides.

Administration of penicillin in patients with ulcerative colitis who have received the drug previously does not reduce the number of fecal bacteria. *E. coli* remains predominant during treatment.

Oral doses of streptomycin in patients who have not previously received streptomycin therapy decrease the number of aerobic fecal bacteria considerably and alter the type of flora. The changes persist for 7 days or less. Organisms growing under anaerobic conditions are not significantly reduced in number.

Oral doses of aureomycin reduce the number of fecal aerobic organisms and alter the predominant organisms. In the quantities given, these changes persist no longer than 8 to 10 days. The number of organisms growing under anaerobic conditions diminished in 9 of 10 cases for periods of 3 to 10 days.

With 2 exceptions, oral administration of chloramphenicol did not significantly lower the average number of fecal aerobic organisms in patients with chronic ulcerative colitis; however, the type of flora was altered temporarily in most instances. The effect of chloramphenicol on fecal anaerobic bacteria could not be evaluated conclusively.

Average aerobic fecal bacterial counts seemed to rise consistently above control levels after varying periods of oral administration of penicillin, streptomycin, aureomycin, and chloramphenicol. A fecal bacterial flora resistant to penicillin, sulfonamides, streptomycin, aureomycin, and chloramphenicol develops more or less rapidly after the continued administration of these drugs. A similarly resistant flora developed in normal persons given sulfaguanidine and oral doses of penicillin and aureomycin.—[Authors' summary.]

See also Section Psychiatry, Abstract 1703.

LIVER

1610. **Venous Hums in Hepatic Cirrhosis**
H. G. J. BLOOM. *British Heart Journal* [*Brit. Heart J.*] **12**, 343–350, Oct., 1950. 3 figs., 32 refs.

Two cases of cirrhosis of the liver in which a venous hum was noted over the xiphisternum, spreading in one case to the right side of the chest and right hypochondrium, are described. The murmur was a continuous loud roar, accompanied by a thrill and abolished by firm pressure on the abdominal wall just below the xiphisternum. In one case a varicose vein could be seen at the site of the hum, and at necropsy a dilated vessel was found connecting the left portal vein with the internal mammary veins.

The literature is reviewed from the time of Laënnec's original description (1819), and the view is put forward that the hum only occurs in the presence of hepatic fibrosis and is heard over a patent umbilical or dilated para-umbilical vein. It must be distinguished from venous hums heard, usually in anaemic subjects, over the inferior vena cava just above and to the right of the umbilicus, over an enlarged spleen or a liver affected by malignant tumour, an abdominal arteriovenous aneurysm, a fibroid, and the uterine souffle in pregnancy, and occasionally from continuous murmurs in the chest.

J. W. Litchfield

1611. **A Study of Dietary Factors, Alcoholic Consumption and Laboratory Findings in 100 Patients with Hepatic Cirrhosis and 200 Non-cirrhotic Controls**
A. Y. OLSEN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 477–484, Nov., 1950. 5 figs., 37 refs.

Cirrhosis of the liver cannot be induced by simple alcoholism, however intense and consistent such a practice may be. But a chronic alcoholic is in danger of developing cirrhosis of the liver if, in addition to steady addiction to beer, wine, or spirits, he is also possessed of an inherent constitutional weakness of his liver cells. Such weakness is of mysterious and quite unknown origin, but it can be clearly demonstrated in familial histories. He must also ruin his appetite and deprive himself constantly of first-class protein and the whole of the vitamin-B complex substances and he must lay

himself open to hepatotoxic attack, including virus infection and the possible direct toxic action of contaminants in alcoholic beverages. *G. F. Walker*

1612. **Amino Acids in Plasma and Urine of Patients with Hepatitis before and after a Single Infusion of Protein Hydrolysate**
J. B. KIRSNER, A. L. SHEFFNER, W. L. PALMER, and O. BERGEIM. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 735–740, Nov., 1950. 18 refs.

The concentration of amino-acids in blood and urine was determined microbiologically in 3 patients and one normal control before and after a single infusion of protein hydrolysate. One patient had mild infective hepatitis with normal hepatic function, the second had portal cirrhosis with severe impairment of hepatic function, and the third biliary cirrhosis with severe acute hepatitis. The normal subject excreted about 51% of the injected nitrogen during the injection period, and 11% of the amino-acids were excreted as such, though in proportions different from those in the preparation injected. Thus 26·6% of injected histidine appeared, but only 4% of leucine. Similar results were obtained in the first 2 patients, but the third excreted only 2·2% of the injected amino-acids. The blood amino-acid level rose only slightly during and after the injection in the control subject and the first and third patients, but a more significant rise occurred in the second. The plasma methionine level was found to be raised in 5 cases of severe active hepatitis, averaging 12 times the normal. But normal plasma methionine values were found in cases of mild healing and healed hepatic disease.

It is concluded that, with the possible exception of methionine, amino-acids are metabolized adequately in the presence of severe liver disease. *C. L. Cope*

1613. **Lipotropic Agents in Liver Damage produced by Selenium or Carbon Tetrachloride**
E. A. SELLERS, R. W. YOU, and C. C. LUCAS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 118–121, Oct., 1950. 14 refs.

Experiments were carried out on groups of female rats fed on a basal diet estimated to contain adequate quantities of known essential amino-acids. One group of rats were given 20% carbon tetrachloride (CCl_4) in corn oil orally in doses of 0·2 ml. three times a week for 8 weeks. Another group received sodium selenate added to the diet in a concentration of 20 parts per million. Each main group was divided into four: a control group and subgroups receiving respectively 0·15% choline chloride, 0·5% DL-methionine, and 0·4% cystine. No protective effect against liver damage by CCl_4 was observed, but there was some protection in all three subgroups against selenium. Repetition of this experiment was not successful and a further investigation was carried out, in which the effects of the same amounts of selenium were studied in subgroups of rats given the same basal diet with supplements of 0·05% α-tocopherol, 0·5% methionine, and both tocopherol and methionine. Histological studies and estimations of the total liver lipid content were made. The results indicated that neither α-tocopherol nor methionine alone protected against liver damage, whereas the two together gave considerable protection.

The significance of this finding is briefly discussed. The authors suggest that "α-tocopherol enables the potential —SH group of methionine to remain 'free' and take part in a detoxification reaction." The failure of choline to give protection indicated that the lipotropic activity of methione was not the significant factor. *B. G. Maegraith*

1614. **Adrenal Cortex in Liver Disease**
J. J. WEBSTER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 854–864, Oct., 1950. 37 refs.

Believing that adrenal cortical hormone, through its action on carbohydrate metabolism and particularly on glycogenesis, might be of value in liver disease, the author studied the effect of an aqueous and an oily extract of adrenal cortex, the respective potencies of which were equivalent to 0·4 to 0·5 mg. and 4·0 to 4·5 mg. of cortisone per ml. The treatment of 9 cases is reported, these being diagnosed as follows: cirrhosis, 4 cases; homologous serum jaundice, 1 case; chronic active infective hepatitis, 1 case; chronic hepatitis with "pseudo-biliary colic", 1 case; arsenical hepatitis, 2 cases. The duration of illness varied from 3 months to 6 years. All the patients had jaundice and hepatomegaly with other clinical and biochemical evidence of severe liver damage; 3 had ascites; none had improved after 2 to 4 weeks or more of routine treatment consisting of bed-rest, high-protein–high-carbohydrate diet, transfusion of blood, plasma, albumin, or glucose, and in some cases administration of "lipotropic factors". Adrenal cortical extract was given daily for periods of 5 to 21 days, and in 6 cases at longer intervals for subsequent periods of 2 weeks to 3 months.

Improvement was obvious within 2 to 7 days, and recovery apparently complete in a few weeks in every case. One patient died of bronchopneumonia and metastatic carcinoma, and another of coronary thrombosis, 7 months and 1 year respectively after completing treatment; the remaining 7 showed no evidence of liver disease after 1 year. Two patients developed transient glycosuria, and a third persistent diabetes; psychic stimulation was regularly noted and in one case treatment had to be stopped because of the onset of mania; it is stated that 2 patients became hypertensive and 2 had precordial pain. Liver biopsy was not undertaken, on the grounds that the patients were too ill, nor are necropsy findings in the 2 fatal cases given.

[The results reported here are striking, but the authority of the paper is diminished by the absence of any histological evidence in support of the clinical and biochemical findings.] *H. McC. Giles*

1615. **A Critical Review of Changes in Liver Function during Liver Disease**
C. H. GRAY. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **19**, 263–276, Oct., 1950. 2 figs., 49 refs.

See also Section Pathology, Abstract 1467.

Endocrine Disorders

1616. **Changes in Renal Function in Man due to Disease of the Anterior Lobe of the Pituitary**
M. PICKFORD and J. A. WATT. *Journal of Endocrinology* [*J. Endocrinol.*] **6**, 398–404, July, 1950. 3 figs., 14 refs.

The renal clearance of inulin and diodone or urea was measured in 10 normal men and women, in 20 patients with various disorders of the anterior pituitary, and in a miscellaneous control group of 14 patients suffering from various hypothalamic, endocrine, and other disorders. In some cases the diuretic response to the ingestion of 500 ml. of water was also measured.

In 5 out of 8 patients with chromophobe adenoma of the pituitary the clearance values were abnormally low; in the other 3 the clearances were normal. In both of 2 patients with the Lorain syndrome the clearances were low. In 1 of 2 patients with exophthalmic ophthalmoplegia, the values were normal, while in the other the glomerular filtration rate (G.F.R.) was normal, but the renal plasma flow (R.P.F.) was reduced. In 2 out of 5 cases of acromegaly the clearance values were low, those in the other 3 being normal; in none of them was the urea clearance above the normal range, in contrast to the findings of Barnett *et al.* (*Proc. Soc. exp. Biol. N.Y.*, 1943, **52**, 114). In the control group, 2 patients who had previously undergone operations in the hypothalamic region and one patient with anorexia nervosa gave normal clearance figures, and one patient with untreated Addison's disease and one with retrobulbar neuritis (in whom necropsy showed a normal pituitary gland) gave low figures. In the remainder, comprising cases of treated Addison's disease and hyperthyroidism, myxoedema, diabetes insipidus, and osteoporosis, the clearances were normal. Water diuresis was markedly impaired in each of 4 cases of chromophobe adenoma tested, and in one untreated case of acromegaly; in a second patient with acromegaly, who had received a full course of *x*-ray therapy, it was normal.

The authors point out the close similarity between their findings in hypopituitarism in man and those following hypophysectomy in dogs and discuss the suggested association of the renotrophic action of the anterior pituitary with the growth-hormone.

Robert de Mowbray

1617. **Investigations on the Urinary Excretion of Corticoids and 17-Ketosteroids during the Administration of Adrenocorticotrophic Hormone (ACTH).** [In English]
M. SPRECHLER. *Acta Endocrinologica* (*Copenhagen*) [*Acta endocrinol., Kbh.*] **5**, 101–142, 1950. 12 figs., 41 refs.

Adrenocorticotrophin (ACTH) was given to a series of patients of both sexes and practically all age groups who were suffering from a variety of conditions including acute and chronic rheumatism, leucoderma, scleroderma, disseminated lupus erythematosus, and Boeck's sarcoid. The ACTH was from four different batches and the dose was usually between 30 and 100 mg. daily, given in 3 or 4 divided doses. The treatment was continued for periods ranging between 4 and 125 days. Urine was collected in 24-hour lots and was assayed for 17-ketosteroids, corticoids, and occasionally glucocorticoids. Ten patients showed a normal response: the urinary excretion of steroids increased on the first day of treatment and continued to increase progressively to reach a maximum on the 3rd to 5th days, then remaining fairly constantly elevated; the excretion of corticoids generally reached a maximum before that of 17-ketosteroids, and the relative increase in the excretion of corticoids was generally greater than that of 17-ketosteroids. In 4 other cases there was a poor response similar to that observed in Addison's disease, but none of these patients had any symptoms of Addison's disease.

A further series of 5 patients were given larger doses of ACTH, varying between 980 and 2,700 mg. daily, during periods ranging between 14 and 23 days. The excretion of urinary steriods was at a high level, but after 9 or 10 days the excretion of corticoids decreased, suggesting an inadequate adrenal cortical reserve. One of these patients, however, although given the high dosage, had only a very poor response throughout the period of treatment. Finally, 5 patients were treated for longer periods varying between 26 and 125 days. In only 2 was there some evidence suggesting that a refractory state developed after about 40 and 70 days respectively.

From the available data it is concluded that the minimum effective daily dose of ACTH required to produce an increased corticoid output is about 5 to 6 mg. in children and about 12 mg. in adults. The corresponding dosage required to produce an increased 17-ketosteroid output is about 12 mg. in children and 14 mg. in adults.

A. C. Crooke

1618. **Effect of Cortisone and ACTH on Eosinophils and Anaphylactic Shock in Guinea Pigs**
M. DWORETZKY, C. F. CODE, and G. M. HIGGINS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 201–206, Oct., 1950. 4 figs., 12 refs.

Guinea-pigs were used throughout this study. The number of eosinophils in the blood of males was significantly lower than that in females. Cortisone reduced the number of eosinophils in the blood of males and females. ACTH produced a pronounced eosinopenia in males and nonpregnant females. Pregnancy abolished the eosinopenic effect of ACTH. Neither cortisone nor ACTH had any effect upon the degree of anaphylactic shock produced in guinea-pigs by the intravenous injection of the agent to which the animals had been sensitized. —[Authors' summary.]

1619. **The Antipyretic Effect of Cortisone**
L. RECANT, W. H. OTT, and E. E. FISCHEL. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 264–266, Oct., 1950. 11 refs.

A series of 48 rabbits, subdivided into cortisone-treated and control groups, were injected intravenously with pneumococcus or *Pseudomonas* vaccines in order to produce an artificial pyrexia. In rabbits previously treated with cortisone acetate in doses of 2·5 to 10 mg. daily for 3 to 10 days the pyrogenic response was significantly lower than in controls. *G. Ansell*

1620. **Suppression of the Phenomenon of Local Tissue Reactivity by ACTH, Cortisone and Sodium Salicylate**
G. SHWARTZMAN, S. S. SCHNEIERSON, and L. J. SOFFER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 175–178, Oct., 1950. 14 refs.

Local tissue reactions were produced in rabbits by injecting intradermally 0·25 ml. of a meningococcus culture filtrate, and then, 24 hours later, injecting intravenously a large "provocative" dose of the material. This resulted in severe, strongly positive, local reactions in 61 out of 71 control animals.

Cortisone (75 mg. per kg.), injected intramuscularly 2 hours before the provocative dose, inhibited the reaction in 4 out of 6 rabbits, and adrenocorticotrophin (12·5 mg. per kg.) produced inhibition in 14 out of 16 rabbits. Sodium salicylate (1·6 g. per kg.) was effective in 17 out of 29 animals. Calcium pantothenate alone had no effect on the reaction, but when it was combined in a dose of 0·4 g. per kg. with sodium salicylate (1·6 g. per kg.) the tissue reaction was suppressed in all 10 rabbits treated. Sodium salicylate also augmented the action of suboptimal doses of cortisone.

A large variety of other substances tested, including deoxycortone acetate and ascorbic acid, failed to influence the local tissue reaction. It is suggested that sodium salicylate and calcium pantothenate may act indirectly through the adrenal cortex, and that a clinical trial with these substances might be undertaken in those diseases associated with alterations in vascular reactivity.
G. Ansell

THYROID GLAND

1621. **Cerebral Disturbances in Myxoedema.** (Les lésions cérébrales du myxoedème)
J. DECOURT, J. GRUNER, and J. LAPRESLE. *Annales de Médecine* [*Ann. Méd.*] **51**, 352–378, 1950. 6 figs., 23 refs.

A histological study of the brain was carried out in 2 cases of severe myxoedema. The first was that of a woman of 48, whose disease had started at the age of 29 without evident cause. When first seen 5 days before death she was somnolent and unable to understand questions, and bilateral extensor plantar responses and bilateral grasp reflexes were obtained. There was no response to administration of thyroid. The second case was that of a woman of 72, who died of uraemia resulting from epithelioma of the bladder and had had long-standing myxoedema.

Details of the post-mortem findings in both cases are given, and the changes in the nervous system are fully described. Lesions were found in the pyramidal cells of the cortex, in some basal nuclei, and in the hypothalamus. There was calcinosis of the vessels of the globus pallidus. Cerebral arteriosclerosis was relatively mild. The vascular changes are described in detail and some are considered to be of myxoedematous origin. Abnormal iron deposits in the brain were also found. In general the abnormalities found were similar to those usually found in the brains of cretins and myxoedematous idiots.
C. L. Cope

1622. **Radiation Dosimetry in the Treatment of Functional Thyroid Carcinoma with I^{131}**
L. D. MARINELLI and R. F. HILL. *Radiology* [*Radiology*] **55**, 494–502, Oct., 1950. 2 figs., 17 refs.

This paper, an exercise in the calculation of tissue doses produced by the presence of radioactive iodine in the body, comes from the Sloan-Kettering Institute, New York City. It is primarily concerned with the estimation of the dosage delivered to secondary thyroid tumour tissue, but the dose delivered to normal tissue, including the blood, the kidney, the stomach, and the mouth, is also discussed. [For details of the calculations involved, with the assumptions that are implicit in them, the paper must be consulted in the original.]
Edward M. McGirr

1623. **Observations on the Prolonged Medical Management of Toxic Diffuse Goiter with Thiouracil and Propylthiouracil**
S. U. GREENBERG and M. BRUGER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 373–380, Oct., 1950. 27 refs.

At New York University–Bellevue Medical Center 70 patients with diffuse toxic goitre were treated with either thiouracil or propylthiouracil, Usually the initial dose of thiouracil was 600 mg. daily, reduced to 300 mg. daily when the basal metabolic rate became normal. The minimum maintenance dose ranged from 50 to 100 mg. daily. From 1946 onwards propylthiouracil was used exclusively. In the earlier stages of treatment the dosage was half that of thiouracil, but the maintenance dose was seldom smaller than 50 to 100 mg. daily.

An adequate course of treatment lasting 1 year was completed in 47 cases, but the subsequent follow-up was inadequate in 8. Of the remaining 39 patients remissions lasting more than 6 months occurred in 30 cases and more than 1 year in 25 of these, while 9 patients suffered a relapse after the cessation of treatment. Of the 23 patients who did not complete the full course of treatment it was found necessary to discontinue the drug in 8 cases owing to the development of severe granulocytopenia, and in one because of muscular weakness. Granulocytopenia of varying degrees of severity developed in 19 of the 37 patients who received thiouracil, but in

only 7 of the 46 who received propylthiouracil. A favourable granulocyte response was elicited by giving these patients pyridoxine hydrochloride by mouth in a dosage of 60 to 225 mg. daily. Twenty-seven patients were examined for evidence of alteration in the size of the thyroid gland. Enlargement of the gland was observed in 2 patients, but the enlargement was insufficient to produce pressure symptoms. A decrease in the size of the gland occurred in 13 cases. No increase in proptosis was detected.

The authors consider that propylthiouracil therapy may be given effectively for periods longer than 1 year in cases in which thyroidectomy is either refused by the patient or contraindicated by the adverse circumstances of the case, or if it is considered that interruption of treatment is likely to prove hazardous owing to the presence of severe complications. *A. Garland*

1624. **Index of Thyroid Function : Estimation by Rate of Organic Binding of ^{131}I**

G. E. Sheline and D. E. Clark. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 450–455, Sept., 1950. 15 refs.

This test of thyroid function is based on the distribution of radioactive iodine (^{131}I) between the protein-bound and inorganic fractions of the plasma, 24 hours after an oral dose of 50 to 200 μc. This is expressed as the conversion ratio $= \frac{\text{protein-bound plasma } ^{131}I}{\text{total plasma } ^{131}I} \times 100$.

Plasma proteins are precipitated from 2 ml. of plasma by adding 8 ml. of 10% trichloroacetic acid. The precipitate is washed twice with 4 ml. of 1% trichloroacetic acid and then dissolved in 4 or 5 drops of 2 M NaOH. After dilution with distilled water the dissolved precipitate is spread evenly in a flat dish and dried under an infrared lamp before measurement of the radioactivity.

The conversion ratio in 28 euthyroid subjects ranged from 3 to 41%. In 13 thyrotoxic cases the range was 45 to 97%. In 3 mildly thyrotoxic patients the conversion ratios were 35, 35, and 38% respectively.

G. Ansell

SUPRARENAL GLANDS

1625. **The Excretion of Urinary Neutral 17-Ketosteroids following Bilateral Splanchnicectomy and Right Adrenalectomy**

E. A. Michie and B. E. Clayton. *Journal of Endocrinology* [*J. Endocrinol.*] **6**, 423–425, July, 1950. 1 fig., 13 refs.

An investigation into the urinary excretion of neutral 17-ketosteroids was carried out in the Clinical Endocrinology Research Unit (M.R.C.) at the University of Edinburgh, on 2 women, aged 48 and 39 respectively, before and after undergoing sympathectomy for hypertension. Bilateral splanchnicectomy was performed in both cases, the greater splanchnic nerve being divided, the sympathetic chain removed from T8 to L3, and all communications to the coeliac ganglion from the spinal nerves divided just short of the ganglion. In one patient the right adrenal gland was also removed. The operation was performed in 2 stages with an interval of more than 10 days; repeated estimations were made of 17-ketosteroid excretion over a control period before operation (15 weeks in one case and 2 weeks in the other), during the interval between the two stages of the operation, and for 4 to 8 weeks subsequently. Fluctuations in 17-ketosteroid excretion which usually occur after operation or trauma were thus allowed for.

Forbes *et al.* (*J. clin. Endocrinol.*, 1947, **7**, 264) observed an initial rise in 17-ketosteroid excretion after various forms of trauma, followed by a fall and return to normal within 10 days, but this was not found in the 2 cases reported here. Although there was considerable day-to-day fluctuation in 17-ketosteroid excretion (mainly between 4 and 12 mg. daily in one patient and between 3 and 6 mg. daily in the other), the operation had no significant over-all effect on the level of excretion. Since the operations involved complete division of the nerve-supply to the adrenals in both cases, and in one case the removal of one adrenal as well, it would appear that the excretion of 17-ketosteroids is not under nervous control, and that when one adrenal is removed the other can compensate for it adequately.

Robert de Mowbray

1626. **The Effects of Adrenaline on the Number of Circulating Eosinophils and on the Excretion of Uric Acid and Creatinine.** [In English]

O. J. Broch and H. N. Haugen. *Acta Endocrinologica* (*Copenhagen*) [*Acta endocrinol., Kbh.*] **5**, 143–150, 1950. 8 refs.

From the results obtained in a series of 23 control subjects and 6 patients with Addison's disease who were given subcutaneous injections of 0·3 to 0·5 mg. of adrenaline, it was concluded that the changes in the number of circulating eosinophil cells and in the concentration of uric acid 4 hours afterwards were too variable to serve as a useful clinical test of adrenal cortical function.

A. C. Crooke

1627. **Capillary Resistance and Adrenocortical Activity**

H. N. Robson and J. J. R. Duthie. *British Medical Journal* [*Brit. med. J.*] **2**, 971–977, Oct. 28, 1950. 7 figs., 22 refs.

In these studies the Scarborough negative-pressure method of determining capillary resistance was used throughout. The apparatus and technique are described. The effects of heat, cold, ultraviolet radiation, *x* rays, nitrogen mustard, histamine, and T.A.B. vaccine on capillary resistance are briefly reviewed. The authors observed a rise in capillary resistance after a dose of adrenaline or insulin.

In 6 patients with rheumatoid arthritis, a single dose of 25 mg. adrenocorticotrophin (ACTH) caused a significant rise in resistance in 4 hours, with a delayed response in one case. With doses of 25 mg. every 8 hours capillary resistance reached a maximum in 72 hours and continued at this level until administration stopped. The resistance then fell at varying speeds, generally returning to basal levels in 10 to 14 days. The extent and speed of the

rise, however, did not always coincide exactly with the percentage fall in eosinophils in the blood. In two cases of spondylitis ankylopoietica, and in one out of 2 cases of disseminated lupus erythematosus, resistance also increased after ACTH therapy. Definite clinical remission on three occasions followed the use of ACTH in 2 cases of idiopathic thrombocytopenic purpura. It is suggested that the rise in capillary resistance might be due to adrenocortical stimulation by endogenous adrenaline or some similar mechanism, and that capillary resistance estimations may be used as a measure of the response of the adrenal cortex to stimulation.

Norval Taylor

See also Section Paediatrics, Abstract 1522.

GENITAL GLANDS

1628. **Fertility in Paraplegic Males. A Preliminary Report of Endocrine Studies**

E. BORS, E. T. ENGLE, R. C. ROSENQUIST, and V. H. HOLLIGER. *Journal of Clinical Endocrinology* [*J. clin. Endocrinol.*] **10**, 381–398, April, 1950. 5 figs., 31 refs.

Testicular biopsy specimens were taken from 34 men with injuries completely or partially transecting the spinal cord at various levels. Only 3 of the specimens were histologically normal; these were from patients with incomplete transection at C5 and complete transection at D4 and D11 respectively. In general, injury at lower levels was associated with a lesser degree of testicular damage than injury at higher levels. The most common abnormality (22 cases) was secondary atrophy, characterized by greatly reduced cell population, generalized pyknosis, and absence of mitoses in any germinal layer. The interstitial cells were usually normal. There was no relation between the degree of atrophy and the time elapsing since injury, nor was damage related to infection or epididymitis. Most of the men were capable of erections, and this capacity had no connection with the state of the interstitial cells.

Sweating tests were carried out in 29 of the men to determine the extent of damage to the cholinergic sympathetic fibres leaving the cord by the anterior roots. This test does not necessarily reveal damage to the adrenergic fibres regulating circulation and temperature in the testes, as the roots by which these leave the cord is disputed. In 5 cases a normal testis was associated with severely impaired sweating or vice versa, but the degrees of impairment of sweating and of testicular atrophy corresponded in the remaining 19 cases. This indicates some direct relation between the testicular condition and the state of the autonomic nervous system, and it is suggested that the atrophy is caused by abnormally high temperature and is analogous to that occurring in cryptorchidism. One patient had a moderate degree of atrophy and only 600,000 immotile sperm per ml. of semen obtained by prostatic massage; half-hour applications of an ice-bag to the testes thrice daily for 3 months increased the count to 33,000,000 per ml.—4% being motile.

Another factor possibly concerned in the testicular damage is adrenal cortical overactivity, which might be induced in response to alarming stimuli, such as urinary infection, decubitus ulcers, and spinal shock, which are common in paraplegics. Some evidence for such overactivity is provided by urinary hormone estimations: the androgen and oestrogen excretion was abnormally high in the majority, while urinary gonadotroph in elimination was low.

Peter C. Williams

1629. **Pregnenolone**

E. HENDERSON, M. WEINBERG, and W. A. WRIGHT *Journal of Clinical Endocrinology* [*J. clin. Endocrinol.*] **10**, 455–474, April, 1950. Bibliography.

Pregnenolone (the 3-hydroxy derivative of progesterone) was prepared in the laboratory in 1934 and isolated from hog testis in 1943. In experimental animals it favours spermatogenesis without affecting the interstitial cells of the testis, and protects the testis against the damaging action of oestrogen. Unfortunately the effect on spermatogenesis is a maintaining and not a curative one—it prevents the loss of spermatogenesis after hypophysectomy, but will not restore it once it is lost. In doses usual for steroids it has no oestrogenic, androgenic, or adrenal-cortical activity, but all these activities can be demonstrated with massive doses in particular types of experiment. It has no toxic action; mice survive single doses of 5 g. per kg. body weight without any ill effect, and very large doses can be repeatedly given during long periods without affecting their growth or fertility, or altering the blood picture.

The clinical application of pregnenolone has so far been empirical. It was first given to volunteers subjected to fatigue in experimental conditions under which the urinary 17-ketosteroid excretion is increased. This increase and other objective signs of fatigue were lessened by giving 50 mg. of pregnenolone daily by mouth. This effect has not been generally confirmed—the drug is apparently only of benefit in fatigue associated with an element of urgency or anxiety. The 17-ketosteroid excretion is increased in ankylosing spondylarthritis and can be reduced to normal by giving 50 to 150 mg. of pregnenolone daily by injection; the treatment reduces pain and muscle spasm and extends the limits of movement. In rheumatoid arthritis the 17-ketosteroid excretion is normal, but the fatigue incident to the condition suggested that the steroid might be of some benefit. Conflicting clinical reports of its effect are summarized, some of which claim relief of pain, lessening of fatigue, and in some cases measurable reduction in swelling. High dosage seems to be necessary and daily doses of 1 g. by mouth or 600 mg. by injection have been given for long periods without any side-effects being noted. Further investigation is warranted, but definite benefit has not yet been proved. The compound has no significant effect on oligospermia.

The authors point out that until a normal physiological role has been assigned to the steroid its use will remain empirical, which the remarkable absence of effects on the rest of the endocrine system makes relatively harmless.

Peter C. Williams

Dermatology

1630. **Bacterial Flora of the Normal Human Skin**
C. A. Evans, W. M. Smith, E. A. Johnston, and E. R. Giblett. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 305–324, Oct., 1950. 5 figs., 30 refs.

Extensive cultural investigation of organisms on the skin of the scapular and deltoid regions showed that anaerobic organisms were 10 to 100 times more common than aerobic. The acne bacillus was most frequently found, but *Staphylococcus albus*, *Micrococcus epidermidis*, and *M. candidus* were regularly present. *Staph. aureus* was not encountered frequently. The subaceous glands and secretion were the chief sites of bacterial growth. The findings in children differed considerably from those in adults. Certain bacteria in culture exerted an inhibitory effect upon the growth of others and probably exercise a similar antibiotic activity on the skin. Lack of bathing and the taking of exercise did not materially affect the bacterial population of the skin.

John T. Ingram

1631. **Sodium *para*-Aminobenzoate Therapy of Atopic Dermatitis. Preliminary Report**
A. L. Weiner. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 295–296, Oct., 1950. 4 refs.

Treatment of 16 patients with atopic eczema with sodium *para*-aminobenzoate produced improvement in 8 cases. A dose of 2 g. was given by mouth every 2 hours during the day. *John T. Ingram*

1632. **Atopic Dermatitis. II. Role of the Sweating Mechanism**
L. Tuft, H. S. Tuft, and V. M. Heck. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 333–337, Oct., 1950. 5 refs.

Inhalation of allergens, alternaria powder in one case and ragweed pollen in another, provoked sweating, itching, and eczematization in flexural sites in 2 patients suffering from atopic eczema.

Histology showed only occasional plugging of sweat ducts. It is suggested that this disturbance of sweating may play some part in the aetiology of eczema.

John T. Ingram

1633. **The Treatment of Psoriasis as a Disturbance of Lipid Metabolism. Further Observations on Lipotropic Therapy based on a Ten-year Clinical Study**
P. Gross and B. M. Kesten. *New York State Journal of Medicine* [*N.Y. St. J. Med.*] **50**, 2683–2686, Nov. 15, 1950. 12 refs.

The authors have made a clinical study of psoriasis and its response to lipotropic therapy over a period of 10 years. In preliminary trials the administration of synthetic choline and inositol did not produce the effect on psoriasis observed after the administration of soy-bean lecithin, which contains choline and inositol as well as essential fatty acids and biotin. A series of 235 patients were treated with a diet low in animal fats and cholesterol, with soy-bean lecithin by mouth and topical therapy (with "vaseline", "vioform", ammoniated mercury, and coal-tar ointments). The soy-bean lecithin supplied approximately 0·6 g. each of choline and inositol daily. Some patients were also given capsules containing 500 mg. of crude lecithin and small amounts of vitamins A and D, aneurin, pyridoxine, riboflavine, and calcium pantothenate. If alcoholism or liver disease was present, crude liver extract and a high protein diet were given. Of 155 patients treated adequately (for an average period of 1 year), of whom 12 were children, 23 were cured and remained free from recurrence for an average period of observation of $2\frac{1}{2}$ years; in 29 of the remainder the disease was "controlled", though there were a few persistent lesions; 66 patients are classed as "improved", and 37 "unimproved". The remaining 80 patients were unco-operative or were not observed long enough for results to be evaluated.

In skin from the lesions of 2 patients the cholesterol content was found to be more than three times that of skin from 4 healthy individuals. Of 254 patients in whom the serum cholesterol was determined, in 64 the value was above normal. The serum cholesterol level was determined during and after treatment in 94 cases, in 55 of which it was significantly reduced during treatment, being unchanged in the remainder. There was no correlation between the response to treatment and changes in serum cholesterol level.

[Although the authors regard psoriasis as being due to a disturbance of fat metabolism, the evidence for this is open to criticism.] *S. T. Anning*

1634. **Use of Cortisone and Adrenocorticotropic Hormone in Acute Disseminated Lupus Erythematosus**
L. J. Soffer, M. F. Levitt, and G. Baehr. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 558–573, Oct., 1950. 5 figs., 8 refs.

A series of 14 patients with disseminated lupus erythematosus were treated with cortisone and adrenocorticotrophin (ACTH). On the whole, ACTH was quicker in its action, but its effect terminated very abruptly when it was withheld. All 14 patients showed dramatic improvement in respect of the characteristic clinical features of the disease, namely, fever, weakness, joint pains, characteristic eruption, and cardiovascular changes. There was, however, little change in the biochemical findings in the patients under treatment, the effect apparently being a matter of simple clinical improvement without arrest of the essential disease processes. All 14 patients had some oedema, hypertension, heart failure, and either depression or euphoria. Of the 14 patients one died in convulsions under treatment and one died from an intercurrent unrelated malady; in one

diabetes mellitus developed. Treatment was continued for several months but all the patients who survived promptly relapsed when the treatment was stopped. It is quite clear that considerable further study of this clinical enterprise is needed. *G. F. Walker*

1635. **The Effect of Topical Antipruritic Therapy on Experimentally Induced Pruritus in Man**
F. M. MELTON and W. B. SHELLEY. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 325–332, Oct., 1950. 10 refs.

The authors observed that the intracutaneous injection of 0·05 ml. of a 1 in 100,000 solution of histamine phosphate evoked a degree of pruritus suitable for the experimental evaluation of local antipruritic measures. A freshly prepared sterile, buffered solution of histamine phosphate was employed and 54 topical antipruritic preparations were tested, the histamine in one series being injected 1 minute before, and in the other series 15 minutes after, the application of the antipruritic. No significant effect was observed from any of the applications, the preparations used including many of those, proprietary and non-proprietary, commonly prescribed for the relief of pruritus. *John T. Ingram*

1636. **Observations on the Urinary Excretion of Histamine in Urticaria**
H. M. ADAM, R. B. HUNTER, and T. W. G. KINNEAR. *Quarterly Journal of Experimental Physiology* [*Quart. J. exp. Physiol.*] **36**, 49–59, Sept., 1950. 1 fig., 15 refs.

The effect of the administration to 3 urticarial subjects of histamine by mouth (133 mg.) or by intravenous infusion (5 to 7 mg.) on the urinary histamine content was the same as in normal subjects. Two of the subjects had a severe urticarial reaction several hours after the infusion. No changes were found in the histamine level of plasma or cells in venous or arterial blood following the infusion. The mean daily excretion of free histamine in 9 cases of urticaria was significantly higher than that of a group of 10 normal subjects and a group of 10 patients with other diseases, the higher mean value in the urticarial group being mainly due to the inclusion of 2 acute cases. *F. W. Chattaway*

1637. **The Proteins in Pemphigus Vulgaris. III. The Effect of Infusions of Human Serum Albumin on the Proteins in the Blood Serum of Patients with Pemphigus Vulgaris**
W. F. LEVER and J. G. MACLEAN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **15**, 215–222, Sept., 1950. 4 figs., 10 refs.

Five patients with severe acute pemphigus vulgaris and marked hypoalbuminaemia received from 5 to 21 infusions of human serum albumin solution (with low salt content and 25 g. albumin per 100 ml.) at intervals of 24 to 48 hours. Administration of adequate amounts caused an appreciable rise in albumin level in the serum. The disease was unaffected, but the general condition of the patients was improved. Adequate precautions must be taken to avoid provoking pulmonary oedema (study of cardiac function, dilution of solution with 350 ml. 5% glucose solution, slow infusion over 4 hours, frequent estimation of blood pressure, pulse rate, and respiration rate, and auscultation of chest for râles).
James Marshall

1638. **A Case of Kaposi's Varicelliform Eruption Treated with Aureomycin.** (Beitrag zur Ursache und Behandlung des Eczema herpeticatum)
J. KIMMIG. *Hautarzt* [*Hautarzt*] **1**, 518–519, Nov., 1950. 2 figs.

The case of a child with typical generalized herpes simplex is described. The father of the child had had herpes labialis a short time before, and the virus of herpes simplex was identified in the blister fluid of the child. Penicillin had no apparent effect on the eruption. Aureomycin in a dosage of 125 mg. 4 times a day, given from the 6th to the 8th day of illness, appeared to control the infection, and the skin lesions were healed without scar formation on the 14th day of illness. Slight diarrhoea was noted, presumably due to the aureomycin.
G. W. Csonka

1639. **Disseminated Cutaneous Herpes Simplex (Kaposi's Varicelliform Eruption). Report of a Case complicated by Pregnancy and Herpetic Keratitis and Review of the Literature of Congenital Malformations due to Dermatotropic Virus Infections in the Pregnant Mother**
O. B. MILLER, C. ARBESMAN, and R. L. BAER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 477–490, Oct., 1950. Bibliography.

A case of disseminated herpes simplex with herpetic keratitis occurring during the second to third month of pregnancy is described. The infection had not produced any detectable congenital defect in the infant, who was observed for 9 months. *G. W. Csonka*

1640. **Podophyllin in the Treatment of Cutaneous Carcinoma**
A. B. KERN and H. FANGER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 526–532, Oct., 1950. 5 figs., 15 refs.

Podophyllin resin, which is successful in the treatment of condyloma accuminatum, was tried as a topical application in a case of basal-cell epithelioma of the dorsum of the nose and in a case of squamous-cell carcinoma of the back of the hand. In both cases partial destruction of the carcinomata followed. Histologically, degenerative cell changes in the lesion, with a trend towards greater tumour-cell differentiation later on, showed that the drug interferes in some way with the usual progression of the carcinoma. Neither case, however, was cured and the drug is believed to be unreliable in the treatment of skin carcinoma.
[Similar results have been reported in larger series by other authors.] *G. W. Csonka*

1641. **Squamous Cell Carcinoma Simulating Granuloma Inguinale**
A. B. KERN. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 515–525, Oct., 1950. 8 figs., 10 refs.

Venereal Diseases

1642. **The Preventive Treatment of Congenital Syphilis.** (Über die pränatale Präventivbehandlung der Lues congenita)
A. WIEDMANN and W. LINDEMAYR. *Hautarzt* [*Hautarzt*] **1**, 439–443, Oct., 1950. 6 refs.

A series of 127 syphilitic mothers received penicillin, arsenic and bismuth, or no treatment during pregnancy. In the penicillin series (66) all children were apparently normal at birth, but one showed a weak seropositive reaction, the mother having been first treated at 9 months for secondary syphilis. Among 21 mothers receiving arsenic and bismuth 3 bore clinically syphilitic children and the babies of 2 others were seropositive at birth. In the untreated series (40) 9 children were clinically affected and 21 were seropositive. It is concluded that all pregnant women who have ever had syphilis should be retreated and the authors favour giving a combination of heavy metal, arsenic, and penicillin throughout the second half of pregnancy.

[From the figures given one could argue that penicillin alone is an adequate drug for the prevention of congenital syphilis. It is not mentioned whether a seropositive reaction at birth without clinical or radiological support is taken as prima facie evidence of congenital syphilis. If the mother is seropositive but was treated during pregnancy, such infants need only serological observation; the majority will be seronegative within 3 months, thus showing it to be a harmless transient phenomenon.]
G. W. Csonka

1643. **Penicillin alone in Neurosyphilis: Spinal Fluid Response including a Comparison with Prepenicillin Therapy**
N. R. INGRAHAM, J. H. STOKES, and G. D. GAMMON. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **34**, 566–580, Nov., 1950. 5 refs.

The authors have now treated 603 patients with neurosyphilis with penicillin at the University of Pennsylvania School of Medicine, 124 of whom had paresis, 122 meningo-vascular syphilis, 229 tabes dorsalis, and 128 asymptomatic neurosyphilis. An analysis of their increasing experience has been made almost annually since the first patient was treated in 1943, and 207 patients have now been observed for 3 years or more. Before treatment 74% of patients had a type-III, 13·6% type-II, 3·8% type-I, and 8·6% a normal cerebrospinal fluid. The dose of penicillin was 5,000,000 units or less in 259 cases, and more than this amount in the remainder; 389 patients had only one course and 214 more than one course, while 473 received aqueous penicillin and 130 were given slowly absorbed preparations.

At 1 to 2 years after treatment the spinal fluid was normal or near-normal in 52% of cases, which figure had increased to 72% at 4 to 5 years. The rate of spinal-fluid improvement tended to level off by the third or fourth year and only about 5% of relapses were noted after that time. Increasing the total dose of penicillin or repeating the course did not seem greatly to influence the result. The desired maximum dose which should be given in one course appeared to be in the region of 5,000,000 units, and repetition of the penicillin course only brought about a further 3 to 5% improvement. Procaine penicillin G proved quite as effective as aqueous penicillin G. The results obtained with metal chemotherapy in pre-penicillin days in 146 patients are also presented. It is considered that a similar type of spinal-fluid response was obtained in these cases, but that the maximum effect occurred 2 years later than when penicillin is used. *R. R. Willcox*

1644. **The Spirochaeticidal Value of Soviet Penicillin.** (Спирохетоцидность советского пенициллина)
K. R. ASTVATSATUROV and V. I. LEJBMAN. Вестник Венерологии и Дерматологии [*Vestn. Vener. Derm.*] No. 5, 27–29, Sept.–Oct., 1950.

Russian-made penicillin was used in the treatment of 24 women with primary, and 30 with secondary syphilis, 40,000 units being given 3-hourly by intramuscular injection. Smears were made and examined for spirochaetes at hourly intervals after beginning penicillin treatment. Spirochaetes disappeared after an average interval of 10·6 hours; there was no essential difference from the results of the treatment of 45 cases with American penicillin, in which spirochaetes disappeared after 10·9 hours. Disappearance was noted after an average of 10·8 hours in 13 patients treated with American crystalline penicillin G. The time taken for spirochaetes to disappear depends also upon the nature of the lesion, being longer in ulcerative lesions and in the presence of much infiltration; it also depends upon the age of the patient, the shortest times being found in those below 20 years of age. A Herxheimer reaction occurred in 74% of patients treated with Russian penicillin; its occurrence was usually associated with an acceleration of the rate of disappearance of spirochaetes. During the course of penicillin treatment the spirochaetes showed abnormalities of form and motility. *D. J. Bauer*

1645. **The Relationship between Immobilizing and Spirocheticidal Antibodies against *Treponema pallidum***
F. A. THOMPSON, B. G. GREENBERG, and H. J. MAGNUSON. *Journal of Bacteriology* [*J. Bact.*] **60**, 473–480, Oct., 1950. 12 refs.

Full details are given of an experiment designed to determine the relationship of the spirochaeticidal antibody, capable of rendering suspensions of *Treponema pallidum* non-infective for rabbits when inoculated intradermally, to the immobilizing antibody, demonstrable in the serum *in vitro*. When the suspension of

spirochaetes was treated with a pooled syphilitic serum in the presence of complement, infectivity was lost as the organism became non-motile, the loss of infectivity appearing to occur slightly before the loss of motility. A period of incubation *in vitro* of the mixture of immune serum, spirochaetes, and complement was necessary before the loss of motility and infectivity could be demonstrated. *D. G. ff. Edward*

1646. **The Development and Behavior Patterns of Immunity in Experimental Syphilis**
R. C. ARNOLD, R. D. WRIGHT, and C. P. MCLEOD. *Journal of Venereal Disease Information* [*J. vener. Dis. Inform.*] **31**, 291–293, Nov., 1950. 4 refs.

A group of 37 rabbits with infectious syphilis of 6 to 11 weeks' duration following scrotal inoculation with Nichols strain of *Treponema pallidum* were treated with 14,400 units of sodium penicillin per kg. body weight, given in 48 two-hourly doses. Ten days later the immunity was challenged by a second similar inoculation and it was noted that 27% of the animals developed new chancres, while the remainder had asymptomatic infections, as proved by node-transfer experiments. Immunity was challenged in a like manner in 22 other animals, but on this occasion 6 months after treatment. None of these developed chancres and, although 36% were shown to have asymptomatic infections, no less than 64% were immune. This apparently indicates that immune bodies are formed after clinical cure.

A further group of 34 rabbits with latent syphilis of 8 months' duration were also treated with penicillin and the immunity challenged 10 days later; 53% developed asymptomatic infections and 47% were immune. When 25 more animals with latent syphilis of 8 months duration were treated with penicillin and the immunity likewise challenged 6 months later, node-transfer studies made 4 months after this showed that 57% had a symptomless infection. After a further 2 months (6 months after the spirochaetal challenge) the same animals were re-treated with penicillin and the immunity was given a second challenge 6 months later. Lymph-node transfers made 4 months after this indicated that, by this time, only 31% had become asymptomatically infected.
R. R. Willcox

1647. **Treatment of Gonorrhea with Chloramphenicol (Chloromycetin)**
A. B. GREAVES, G. R. MACDONALD, M. J. ROMANSKY, and S. R. TAGGART. *Journal of Venereal Disease Information* [*J. vener. Dis. Inform.*] **31**, 261–262, Oct., 1950. 7 refs.

A series of 96 male patients with acute gonorrhoea were treated with single doses of chloramphenicol. The criterion of cure was the finding of three negative smears and cultures taken during the comparatively brief post-treatment period of 7 to 10 days; 70 cases were followed up for this period.

Of 4 patients receiving a single dose of 250 mg. only one was considered cured; of 16 given a single dose of 500 mg. 12 were considered cured, and of 50 receiving 750 mg. the outcome was satisfactory in no less than 48.

The danger of masking syphilis by chloramphenicol treatment is considered to be about as great as with penicillin. A single dose of 250 mg. was found to be insufficient to banish *Treponema pallidum* from the positive lesions of primary and secondary syphilis in 3 patients while, out of 2 cases given 500 mg., the spirochaetes were still motile after 96 hours in one, but had disappeared after 48 hours in the other.
R. R. Willcox

1648. **Effectiveness of Antichancroidal Drugs tested by Heteroinoculation of Bubo Fluid from Untreated Donor**
R. R. WILLCOX. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 533–539, Oct., 1950. 1 ref.

Antichancroidal drugs have been tested in 90 volunteers by assessing their power of preventing experimental infection after inoculation with virulent bubo fluid. Of the preparations so tried, sulphathiazole, streptomycin, aureomycin, and chloramphenicol gave efficient protection (of 36 persons, 33 were completely protected, 3 showing doubtful reactions). Antimony, bismuth, and neoarsphenamine proved ineffective. Of the 30 controls, 27 developed a pustule at the site of inoculation. Penicillin was effective only if a high concentration was maintained in the serum. Thus of those receiving a single injection of 2,400,000 units of procaine penicillin in aluminium monostearate, only 50% were " protected " as against 100% of those receiving a daily injection of 600,000 units of penicillin in oil and wax for 8 days. Penicillin (400,000 to 600,000 units over 3 to 4 days) given orally " protected " 3 out of 4 and appears to have some prophylactic value.

[This appears to be a novel way of testing antichancroidal drugs, and provides clear results in a short time.]
G. W. Csonka

1649. **Granuloma Inguinale of the Cervix Uteri and Vulva treated with Streptomycin**
R. H. HOGE and A. M. SALZBERG. *American Journal of Obstetrics and Gynecology* [*Amer. J. Obstet. Gynec.*] **60**, 911–913, Oct., 1950. 2 figs.

Five negresses with granuloma inguinale of the vulva received 13 to 40 g. of streptomycin intramuscularly in divided doses over a period of 4 to 6 days. There were no toxic symptoms and there was subjective improvement in each case within 48 hours, with evident healing by the sixth day. There were no recurrences in a follow-up period of 2 to 10 months. Two women became pregnant; one delivery was normal, although previously the granuloma inguinale had made intercourse impossible; the other was by Caesarean section to avoid injury to the scarred and fibrotic vagina.

Three women with granuloma inguinale of the cervix received 4 g. of streptomycin daily for 5 days. Symptoms disappeared in 2 weeks, and the appearance of the cervix was much improved, although one was left with a small superficial ulcer and in 2 a chronic non-specific cervicitis remained which responded to conization. Pathological examination of the last 2 revealed no Donovan bodies.
Margaret Puxon

Genito-urinary Disorders

1650. **Congestive Heart Failure of Renal Origin. Pathogenesis and Treatment in Four Cases of Carbon Tetrachloride Nephrosis**
C. K. FRIEDBERG. *American Journal of Medicine* [*Amer. J. Med.*] **9**, 164–174, Aug., 1950. 23 refs.

Four cases of carbon tetrachloride poisoning with severe renal damage are described. Three of the patients recovered. In all there had been anuria or oliguria and definite evidence of cardiac failure.

The impairment of renal function—principally the inability to excrete sodium—causes the appearance of congestive failure. All these cases had been made worse by the administration of sodium and fluid, and it is stressed that as these patients usually recover spontaneously it is of the utmost importance not to precipitate cardiac failure by the administration of even small amounts of sodium or an excessive amount of fluid. It is not often realized how small the amount of fluid given must be if this risk is to be avoided. Sodium should be omitted altogether.

Cardiac failure in these cases was thought to fall into the high-output class. Treatment was mainly expectant, because the dangers of overtreating the associated azotaemia, acidosis, hyperchloraemia, and hypernatraemia are considerable. Congestive cardiac failure with pulmonary oedema is the most important complication, as it is the one likeliest to endanger life; it was treated by digitalis administration and phlebotomy.

These findings support the theory that renal dysfunction may be responsible for the clinical picture in cases of cardiac failure in which the primary disease is in the heart. *J. B. Wilson*

1651. **Nephrocalcinosis associated with Hyperchloraemia and Low Plasma-bicarbonate**
A. D. TELFORD GOVAN. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **19**, 277–283, Oct., 1950. 11 figs., 12 refs.

The post-mortem appearances in a 28-year-old woman suffering from nephrocalcinosis are described. A finding not previously reported is of vacuolation of the proximal convoluted tubules, and it is suggested that this change may be of aetiological significance. It is considered that the calcification in the distal convoluted tubule and collecting tubule areas is secondary.
G. M. Bull

1652. **Adult Renal Osteitis Fibrosa with Metastatic Calcification and Hyperplasia of One Parathyroid Gland. Report of a Case**
E. A. DRESKIN and T. A. FOX. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 533–557, Oct., 1950. 9 figs., bibliography.

Hyperplasia of the parathyroid gland may be of one of three main types—simple adenoma, primary hyperplasia (water-clear cell type), and secondary hyperplasia (chief-cell type). Long-standing disease of the kidney tends to promote hyperplasia of the parathyroid glands. This hyperplasia may take any form from simple diffuse and limited hyperplasia of a few portions of the gland to a well-defined palpable adenoma with metastatic calcifications, osteoporosis, and pigmentation of the skin.

The present report is of a case showing these phenomena. There was some improvement on removal of the hyperplastic mass from the gland, but the renal disease progressed and ultimately led to death.

Pigmentation of the skin in disease of the parathyroid gland is apparently more common than has been realized; this point is worthy of more consideration.

[It is quite clear from this case that no patient with renal disease of any duration has been thoroughly examined unless the parathyroid activity has been investigated clinically and biochemically and the skeleton carefully studied radiologically.] *G. F. Walker*

1653. **Report of a Case of Long Standing Renal Insufficiency with Extensive Metastatic Calcifications (Renal Osteitis Fibrosa Cystica)**
R. T. LEVIN and P. D. GENOVESE. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 423–429, Sept., 1950. 9 figs., 14 refs.

The case of a man aged 55, with a history of Bright's disease in childhood, who subsequently developed renal insufficiency and extensive metastatic calcifications, is presented. The unusual features of this case are the prolonged illness and the probable presence of metastatic calcifications 18 years prior to death.

The essential features of secondary hyperparathyroidism due to renal disease have been reviewed.—[Authors' summary.]

1654. **Idiopathic Hyperchloraemic Renal Acidosis of Infants (Nephrocalcinosis Infantum). Observations on the Site and Nature of the Lesion**
A. L. LATNER and E. D. BURNARD. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **19**, 285–301, Oct., 1950. 6 figs., 28 refs.

Investigations were carried out on 6 children suffering from nephrocalcinosis and 5 normal children of comparable age. Acidosis similar in degree to that found in the patients was induced in the controls by acid feeding. To both groups phosphorus was administered intravenously and observations made, at different plasma phosphorus levels, of glomerular filtration rate or urea clearance, urine *p*H, and the excretion of ammonium, phosphorus, and bicarbonate. At high plasma phosphate levels the patients were able to excrete urine of equal *p*H and ammonia content to that of the controls, and there was a marked fall in bicarbonate excretion. These results are interpreted as indicating that the primary defect in nephrocalcinosis lies in the proximal convoluted tubule rather than the distal, as presumed

hitherto. Determination of the partial pressure of carbon dioxide in urine is suggested as a test to detect patients with nephrocalcinosis. Values above 50 mm. Hg in the presence of acidosis are considered to be significant.

[The reasons for the authors' interpretations are too complicated to be adequately summarized, and this interesting and important paper should be read in full.]

G. M. Bull

1655. **Intestinal Lavage in the Treatment of Severe Uraemia.** (Le lavage intestinal dans le traitement de l'urémie grave)

E. E. Twiss. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 4544–4551, Nov. 30, 1950. 5 figs., 25 refs.

If, in the treatment of uraemia by intestinal lavage, the same isotonic rinsing fluid (usually with a sodium chloride content of 0·5 to 0·6%) is used as in peritoneal dialysis, the incidence of pulmonary and general oedema with subsequent cardiac failure and death is rather high. In the author's opinion, which is supported by experimental evidence, it is a mistake to expect the same effect from the intestinal mucosa, with its more differentiated excreting and absorbing capabilities, as from the semi-permeable peritoneum, and the indiscriminate use for intestinal lavage of a rinsing fluid whose isotonicity is based mainly on its salt content is bound to lead to retention of sodium chloride and water. A rinsing fluid suitable for intestinal lavage may be made up as follows: carboxymethylcellulose, 0·3 to 1%; sucrose, 6 to 8%; glucose, 0 to 3·6%; magnesium sulphate, 0 to 2·5%; sodium chloride, 0·1 to 0·15%; potassium chloride, 0 to 0·04%; calcium chloride, 0·028%; sodium bicarbonate, 0·1 to 0·2%. Three patients only have been treated with this fluid, all of them suffering from an irreversible renal insufficiency. A modified Miller–Abbott tube was introduced into the jejunum, and lavage carried out with amounts up to 18 litres of rinsing fluid in 24 hours, in one case once only, but in the others for two periods of 8 days each, the procedure being apparently well tolerated. It proved effective in withdrawing up to 20 g. of urea in 24 hours, but reduced the blood urea concentration less than is usual with Kolff's artificial kidney. All 3 patients died, but the life of each of them was prolonged, perhaps by as much as 2 weeks in one case.

L. H. Worth

1656. **Serum Potassium in Uremia. Report of Sixteen Cases, Some with Paralysis**

W. J. Kolff. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 719–728, Nov., 1950. 2 figs., 23 refs.

High or low serum potassium levels may occur in uraemia according to the method of treatment. The author has seen 9 patients with acute or chronic uraemia in whom the serum potassium level was below 15 mg. per 100 ml. Of these, 8 had been on a high-calorie, low-protein diet. In one case peritoneal lavage reduced the serum potassium level to 7 mg. per 100 ml. and muscular paralysis occurred; this was relieved by giving potassium chloride, a maintenance dose of 2 to 4 g. daily being required for 20 months in those patients who recovered. In another case in which symptoms of potassium deficiency had followed peritoneal lavage, the removal of potatoes from the patient's diet during convalescence precipitated a recurrence of paralysis, with a serum potassium level of 3 mg. per 100 ml. Paralysis was almost complete and included the diaphragm, but the mind was unclouded. Potassium was given and recovery was steady for a few days, but a relapse ensued, leading rapidly to death. The serum potassium level had risen under treatment to 44 mg. per 100 ml. and in this case the symptoms of potassium intoxication were indistinguishable from those due to potassium lack. High serum potassium levels (above 35 mg. per 100 ml.) were found in 7 cases of uraemia. Some of these patients were almost comatose. Muscle weakness was sometimes present and cardiac arrest occurred in 2 cases.

In uraemia a low serum potassium level may be expected when a high carbohydrate diet containing little potassium is given. Maintenance doses of 2 to 4 g. of potassium chloride are required in most cases of uraemia on a high-fat, high-carbohydrate diet. When tissue breakdown occurs rapidly in uraemia, enough potassium may be liberated to cause intoxication. The electrocardiogram has not been found to provide a sufficient guide, and frequent serum potassium determinations are desirable. Death from potassium intoxication is usually sudden and unexpected. Dangerously high serum potassium levels can be lowered by vividialysis or by giving one litre of 40% glucose with 30 units of insulin through a cardiac catheter.

C. L. Cope

1657. **Gastric Perfusion in the Treatment of Chronic Uraemia.** (La perfusione dello stomaco nel trattamento dell'uremia cronica)

M. Baldini, S. Lamperi, and F. Ricci. *Minerva Medica* [*Min. med., Torino*] **2**, 422–427, Sept. 8, 1950. 1 fig., 12 refs.

In 3 patients with chronic renal failure and severe symptoms of uraemia the stomach was washed out over a period of 6 hours with 2 litres of a glucose-saline solution (NaCl 6 g., $NaHCO_3$ 2 g., KCl 0·4 g., $CaCl_2$ 0·3 g., $MgSO_4$ 6 g., glucose 10 g. per l.) by means of a double-lumen stomach tube. The washing was repeated approximately 12 times on alternate days. Occasionally the magnesium sulphate had to be omitted as it caused diarrhoea. A high-calorie, low-protein diet was administered over the same period.

This procedure lowered the blood urea values by some 50%, the quantity of urea removed at each washing ranging from 170 to 516 mg. in the first case, 160 to 400 mg. in the second case, and 70 to 572 mg. in the third. Improvement in the uraemic symptoms was marked, but the power of the kidney to excrete urea was not improved.

James D. P. Graham

1658. **Pergastric Intestinal Perfusion for Uremia**

L. Bernstein, P. B. O'Neill, A. Bernstein, and W. S. Hoffman. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 849–860, Dec., 1950. 3 figs., 23 refs.

Disorders of the Locomotor and Osseous Systems

1659. **The Shoulder–Hand Syndrome and Aortic and Coronary Disease.** (Syndrome "épaule – main" et affections aortocoronariennes)
P. SOULIÉ, R. TRICOT, and M. DEGEORGES. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 4141–4150, Oct. 30, 1950. 10 figs., bibliography.

After a review of the literature on the shoulder–hand syndrome, 4 cases observed by the authors are described. Three of the patients developed the typical signs and symptoms of the syndrome after an attack of myocardial infarction, and the fourth had syphilitic aortitis with severe retrosternal pain and dyspnoea. This last patient died and necropsy revealed, in addition to the cardiac and aortic changes, microscopic lesions of a proliferative type in the region of the last two cervical and first dorsal nerve roots, with some degenerative changes in the corresponding spinal ganglia.

After describing the general course, progress, radiological appearances, and treatment of the condition, the authors discuss its aetiology in some detail. It is considered that the most probable cause is reflex sympathetic inhibition affecting the upper dorsal and stellate ganglia and that this is confirmed to some extent by the post-mortem findings. *Kathleen M. Lawther*

1660. **Vertebral Osteo-arthritis and Rheumatism.** (Spondylosis deformans und Rheumatismus)
U. COCCHI. *Radiologia Clinica* [*Radiol. clin., Basel*] **19**, 351–364, Nov., 1950. 3 figs., 24 refs.

The relationship between spinal osteo-arthritis and rheumatism has not been yet fully explained. Osteo-arthritic changes occur in the vertebrae not only in man but also in erect animals (baboon, kangaroo), and represent not inflammatory but degenerative changes. Inflammatory changes occur in the soft tissue surrounding the vertebral column, and usually follow a throat infection.

The author has studied radiographs of the vertebrae of 1,017 patients. They reveal an increased incidence of osteo-arthritic changes in older patients, this increase being related to the age (in the 2nd decade, 3%; in the 5th decade, 55%; in the 8th decade, 95%).

The occupation of the patient has no material influence on the incidence and degree of osteo-arthritis. No difference was observed between patients with sedentary occupations and those working in the erect position. There was, however, a difference between patients employed indoors and outdoors; in the former osteo-arthritis was found in 49% of cases, and in the latter in 68% of cases. The author attributes this difference to the influence of weather conditions.

Only 78% of patients complained of symptoms related to the spine. In others osteo-arthritis was an accidental finding. Out of 81 patients radiographed because of other symptoms (tumours of the neck, goitre) and without a history suggestive of osteo-arthritis or of any specific or non-specific inflammatory process, half the patients showed no changes in the spinal column and the other half showed osteo-arthritic changes of various degree. There was no difference in radiological appearances between cases with symptoms and those without. The osteo-arthritic changes in the latter group, however, appeared at a later age (4 to 10 years later) than in the former group. Hence radiological evidence of osteo-arthritis is not important from the clinical point of view.

The spine is not uniformly affected, areas most exposed to strain being most commonly involved. These areas are: C 4 to 7, D 5 to 9, and L 3 to 5.

Exposure to adverse weather conditions causes perispondylitis, which accelerates the normal "wear and tear" process in the spine. Perispondylitis improves on treatment, but osteo-arthritic changes remain unaffected by treatment and may even progress.

[The author's tables of results should be studied in the original by those interested.] *W. J. Czyzewski*

1661. **Accessory Sacroiliac Articulations with Arthritic Changes**
L. A. HADLEY. *Radiology* [*Radiology*] **55**, 403–409, Sept., 1950. 9 figs., 3 refs.

Accessory articulations may frequently be demonstrated between the ilium and the posterior surface of the sacrum. These joints may show arthritic changes of lesser or greater degree, and ankylosis may occur. Many of the patients complain of low backache, and some of tenderness when pressure is applied over the accessory joint. Photographs of 2 osteological specimens and radiographs of 6 patients with accessory sacro-iliac articulations are reproduced, illustrating asymptomatic, arthritic, and ankylosed joints. *A. Orley*

1662. **A Further Anatomical Check on the Accuracy of Intra-articular Hip Injections in Relation to the Therapy of Coxarthritis**
M. M. DOBSON. *Annals of Rheumatic Diseases* [*Ann. rheum. Dis.*] **9**, 237–240, Sept., 1950. 4 figs., 4 refs.

The accuracy of intra-articular injection of the hip joint was tested in 40 cases in the cadaver. In 27 the injection was successful, the anterior approach being slightly more reliable than the lateral. *H. F. Turney*

1663. **Chronic Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber–Christian Disease). Relation to Rheumatic Fever and Allied Disease**
J. C. BRUDNO. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 513–517, Oct. 5, 1950. 5 figs., 24 refs.

A case of Weber–Christian disease is recorded. This is an uncommon syndrome characterized by successive crops of nodules in the subcutaneous (and sometimes

internal) fatty tissue, associated with fever. As long as there are nodules present, fever persists. The nodules, single or in clusters and mainly on the thighs, are caused by a focal inflammatory process. Histologically, the early changes are oedema, congestion, infiltration with segmented cells and lymphocytes, necrosis of fat, and phagocytosis of fat droplets by large histiocytes; later there is replacement by collagen, and ultimately fibrosis. The overlying skin is at first red and raised; with involution of the nodule it becomes pigmented and depressed.

The case reported occurred in a woman aged 29, who was admitted to the City Hospital, Quincy, Massachusetts, with migratory joint pain and fever, and gave a past history of rheumatic fever. The author suggests that Weber–Christian disease is not a disease entity, but an allergic reaction with focal manifestations in the subcutaneous or intra-peritoneal fat, and that it is allied to the group of collagen diseases. *Kenneth Stone*

RHEUMATOID ARTHRITIS

1664. **Assessment of Adrenal Cortical Activity in Cases of Chronic Rheumatism after the Intravenous Administration of Large Doses of Sodium Glycerophosphate.** (Esame della funzionalità cortico-surrenale in "reumatici" cronici dopo somministrazione endovenosa di glicerofosfato di sodio ad alte dosi)
P. NATALE and A. PALA. *Policlinico, Sez. Pratica* [*Policlinico (prat.)*] **57**, 1365–1371, Oct. 23, 1950. 20 refs.

After a brief review of the theories of the pathogenesis of chronic rheumatic disorders, Selye's general adaptation syndrome in response to stress, and the alarm reaction, are discussed as being concerned with upsetting the balance of the diencephalic–pituitary–adrenocortical system, thus leading to chronic disorder of the joints. An attempt was made to determine whether the good results of large doses of sodium glycerophosphate are due to its activation of a "stress" mechanism, thereby stimulating the output of cortisone and/or adrenocorticotrophic hormone (ACTH).

Six patients with rheumatoid arthritis and 2 normal controls were given 10 ml. of sodium glycerophosphate (2·5 g. in a 25% solution) intravenously for three consecutive days. Three days before and for 3 days after the injection, Thorn's test was carried out to see if there was any marked drop in the number of the eosinophils in the blood or an increase of the uric acid/creatinine ratio in the urine, indicating an excess of ACTH and/or cortisone. The results showed a complete irregularity before and after the experiment, and have to be regarded as negative. Lucherini's view that the beneficial effect of large doses of sodium glycerophosphate is perhaps due to their influence on the acid-base balance is thought to be nearer the mark.

[A study of the tabulated results of these carefully performed experiments is of much interest. The great variation in the findings even before the injections, and in the controls, should be a warning against wishful thinking and exaggerated hypotheses in connexion with indirect biochemical and biological assays of cortisone and ACTH.] *V. C. Medvei*

1665. **Prolonged Treatment of Rheumatoid Arthritis with A.C.T.H. alone and with Gold**
J. GOSLINGS, W. HIJMANS, P. M. VAN LIMPT, and H. A. VAN GILSE. *British Medical Journal* [*Brit. med. J.*] **2**, 1019–1024, Nov. 4, 1950. 5 figs., 15 refs.

In view of the established observation that the favourable effects of adrenocorticotrophin (ACTH) treatment in rheumatoid arthritis rapidly disappear when it is discontinued, and that with prolonged administration untoward side-effects tend to occur, the authors of this paper set out to find some method of combining a minimal maintenance dose of this material with one of the approved medical remedies in the hope that a remission might be induced and that no relapse would then occur after the discontinuance of the ACTH injections.

With this end in view, they treated 5 patients with rheumatoid arthritis and one with ankylosing spondylitis with small doses of ACTH over periods of 2 to 6 months. In 4 of these cases there was a completely favourable reaction, which it was found possible to maintain with 6 intramuscular injections of 2 mg. of ACTH daily. An attempt was then made to maintain this improved condition with injections of gold salts. Although this procedure would appear to be a reasonable one the authors were unable to decide whether it was successful in their cases, and they state that more experience with the combined treatment will be necessary before conclusions can be drawn. *W. S. C. Copeman*

1666. **Influence of Adrenocorticotrophic Hormone (ACTH) on Differences of Potential Between Synovial Fluid and Skin in Rheumatoid Arthritis**
I. E. STECK, M. M. MONTGOMERY, C. I. REED, and N. R. JOSEPH. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 84–90, Aug., 1950. 7 refs.

In an investigation carried out at the University of Illinois, Chicago, the potential difference between the skin and the synovial fluid of the knee-joint was determined by means of a needle electrode inserted into the cavity of the latter, and a circuit including two standard saturated potassium chloride–calomel half-cells. In 5 young males, aged between 20 and 30, with no evidence of rheumatoid arthritis a difference of potential ranging from 0 to 5 mv. was recorded, the joint potential being positive in relation to the skin, whereas in 6 patients with active rheumatoid arthritis the differences ranged from 28 to 76 mv. during a control period. The joint potential in the latter, however, fell markedly during the first hour after the administration of 25 mg. of adrenocorticotrophin (ACTH), while in all cases the joint potential fell to less than 5 mv. at some time during a course in which 75 mg. of ACTH was given followed by 100 mg. daily for a further 3 days. In 5 cases the potential difference returned to the pre-treatment level on the second or fourth day after cessation of treatment.

From these results it is concluded that "the primary effect of administration of ACTH is a metabolic process

mediated through the adrenal cortex and manifesting itself as a change in bioelectric potential of the articular structures". [Since a number of types of metabolic inhibition are known to result in the production of positive potentials, the problem here posed appears to involve the specificity of the adrenocortical hormones in affecting a given reaction known to yield positive potentials. Further experiments correlating physico-chemical and metabolic processes with potential-difference changes in experimental animals are required.]

A. T. Macqueen

1667 (*a*). **Plasma Levels of Free Amino Acids in Normal Subjects compared with Patients with Rheumatoid Arthritis**

A. L. Borden, E. B. Wallraff, E. C. Brodie, W. P. Holbrook, D. F. Hill, C. A. L. Stephens, L. J. Kent, and A. R. Kemmerer. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 28–30, Oct., 1950. 11 refs.

Considerable evidence is available that abnormal metabolism of amino-acids is a frequent accompaniment of rheumatoid arthritis. The investigation reported by the authors was undertaken in order to determine whether a difference exists in the plasma content of free amino-acids as between normal individuals and patients with rheumatoid arthritis. The levels of free arginine, glycine, histidine, lysine, phenylalanine, serine, and threonine in the plasma of groups of 21 to 40 normal subjects and of 25 to 61 patients are reported upon.

Since it is generally agreed that plasma values for these amino-acids are normally relatively constant, it would be reasonable to suppose that any significant change observed in an adequate series would be worthy of further consideration. It was found that the mean values for arginine, histidine, and threonine in the rheumatoid arthritic patients were very significantly lower than those obtained in the normal groups. The values for glycine, lysine, phenylalanine and serine were not significantly different in the two groups.

W. S. C. Copeman

1667 (*b*). **Urinary Excretion of Certain Amino Acids during ACTH and Cortisone Treatment of Rheumatoid Arthritis**

E. C. Brodie, E. B. Wallraff, A. L. Borden, W. P. Holbrook, C. A. L. Stepehns, D. F. Hill, L. J. Kent, and A. R. Kemmerer. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 285–287, Oct., 1950. 3 refs.

The urinary excretion of free threonine, lysine, tyrosine, and arginine was estimated in 41 patients suffering from rheumatoid arthritis before and during treatment with adrenocorticotrophin (ACTH) or cortisone (on which they all subsequently improved to a varying extent), the excretion values during the control periods being compared with the average and maximum values during treatment. The authors were able to show a highly significant increase in urinary excretion of free threonine, lysine, and tyrosine in patients treated with ACTH, as calculated both from the average and maximum 24-hour excretion. Patients treated with cortisone excreted a highly significantly increased amount of threonine and tyrosine, but not of lysine, at the maximum. Arginine excretion was not increased by either drug. The cause of this increase in urinary excretion of the amino-acids under study is not known, but may possibly be associated with the metabolic changes brought about by the remission of rheumatoid arthritis.

W. S. C. Copeman

1668. **Rheumatoid Arthritis. Partial Rehabilitation by Interval Therapy with A.C.T.H. and Cortisone**

R. E. Stone, T. D. Spies, and W. Niedermeier. *Lancet* [*Lancet*] **2**, 555–560, Nov. 18, 1950. 2 figs., 9 refs.

The continued administration of adrenocorticotrophin (ACTH) may be harmful, as it may over-stimulate the adrenal glands, while that of synthetic cortisone may, on the other hand, result in some degree of adrenal atrophy (as in certain examples of Cushing's syndrome where one cortex is hyperplastic and the other hypoplastic). In view of these facts it seemed worth while to treat a series of cases of active rheumatoid arthritis with a course of ACTH, followed after an interval by a course of cortisone. During the interval, injections of pregnenolone acetate, deoxycortone acetate and ascorbic acid, saline, or salicylic acid were given. Only ACTH and cortisone produced any beneficial effect.

There is no evidence that the fundamental disease process of rheumatoid arthritis is cured by this treatment, but the course of the disease is favourably influenced and all the patients treated obtained temporary remission. The authors suggest that the aim should be to treat each relapse with the minimum amount of hormone required to establish a remission, possibly using ACTH and cortisone alternately.

D. P. Nicholson

1669. **Effectiveness of Cortisone Administered Orally**

R. H. Freyberg, C. T. Traeger, C. H. Adams, T. Kuscu, H. Wainerdi, and I. Bonomo. *Science* [*Science*] **112**, 429, Oct. 13, 1950. 1 ref.

1670. **Observations on the Effect of Cortisone in Chronic Arthritis.** (Beobachtungen über die Wirkung von Cortisone (17-Hydroxy-11-dehydro-corticosteron) bei chronischer Arthritis)

F. Ceresa, G. F. Rubino, and G. Gamma. *Praxis* [*Praxis*] **39**, 923–927, Oct. 26, 1950. 4 figs.

The authors report their observations on the use of cortisone in 2 cases of rheumatoid arthritis and one of acute rheumatic fever. The dosage used was 200 mg. on the first day, with 100 mg. on subsequent days, given intramuscularly. In the cases of rheumatoid arthritis there was dramatic relief of pain, with return of movement and function in the affected joints, within 4 hours of the first injection. In the case of rheumatic fever, which had not responded to salicylates, there was a marked improvement on giving cortisone. In each case there was the usual return to the former state after treatment was stopped.

Cortisone produced in all 3 cases a slight polymorphonuclear leucocytosis, eosinopenia, slight hypertension, a

rise in the blood sugar level of 20 to 30 mg. per 100 ml., and an increase in the urinary excretion of 11-oxysteroids, 17-ketosteroids, and of acid. These changes are listed in detail day by day in all 3 cases before, during, and after treatment. A warning of the possible ill effects of cortisone is given. *G. S. Crockett*

1671. **A Study of Cortisone and other Steroids in Rheumatoid Arthritis**
W. S. C. Copeman, O. Savage, P. M. F. Bishop, E. C. Dodds, B. Gottlieb, J. H. H. Glyn, A. A. Henly, and A. E. Kellie. *British Medical Journal* [*Brit. med. J.*] **2**, 849–855, Oct. 14, 1950. 6 figs., 24 refs.

This study was begun with the object of testing various steroids in cases of rheumatoid arthritis; a small supply of cortisone became available, and the investigation was therefore extended.

Under controlled conditions the various substances were tested, and any one showing therapeutic activity was compared as regards effect with an inert substance, namely, cholesterol. Haematological and metabolic estimations were made at the same time.

Of the steroids used—androstenedione, dehydro-*iso*-androsterone, progesterone, pregnenolone, pregnadienolone, and cortisone—only the last showed significant therapeutic activity. It was given in 5 cases for 10 days; in all cases the response was dramatic.

D. P. Nicholson

1672. **Serum Factor in Rheumatoid Arthritis Agglutinating Sensitised Sheep Red Cells**
J. Ball. *Lancet* [*Lancet*] **2**, 520–524, Nov. 11, 1950. 6 refs.

It was reported by Rose *et al.* (*Proc. Soc. exp. Biol., N.Y.*, 1948, **68**, 1) that serum from cases of rheumatoid arthritis agglutinated sensitized sheep erythrocytes in high dilutions, whereas normal sheep cells were agglutinated only in low dilutions. The author demonstrates that the factor responsible for agglutination in sensitized sheep erythrocytes is not the heterophil antibody, but must be an entirely different and hitherto unrecognized substance. He standardizes the duration of the test and points out that the rabbit anti-sheep-erythrocyte serum used for the sensitization of the sheep cells may not always contain equal proportions of haemolysin and of agglutinin. With a sufficiently wide margin between agglutinin and haemolysin titres, the original technique of standardizing the sensitizing serum on the basis of its haemolysin content is satisfactory, but in rare cases the agglutinin titre of the rabbit serum may be so high as to cause spontaneous agglutination of the sensitized cells. The author therefore checks the haemolysin content against a human serum of which the agglutinin titre for sensitized cells is known.

Out of 286 cases diagnosed clinically as of rheumatoid arthritis, the serum in 49% contained the factor, and in 51% it was negative. The test was negative in 97·6% of 85 cases of ankylosing spondylitis, in 98·3% of 107 cases of osteoarthritis, and in 94·2% of 120 cases of arthritis of other types. Of 79 patients attending a rheumatism clinic suffering from indeterminate painful states such as fibrositis, all but one gave a negative reaction, while 100% negative reactions were obtained in 9 cases of rheumatic fever, 8 cases of acute or subacute rheumatism, and 134 cases of various non-arthritic diseases. Of 67 medical and surgical patients chosen at random, only one gave a positive reaction.

The author concludes that the factor in human serum which agglutinates sensitized sheep erythrocytes and is distinct from heterophil antibody is of considerable serological interest. It seems to be present in relatively small amounts in the sera of some apparently healthy persons as well as in various diseases, but in a proportion of cases of rheumatoid arthritis the concentration of the factor is greatly increased, with the result that the agglutination of sensitized cells may be evident when the serum is diluted a thousand times or more. He suggests that this factor may possibly be related to the disease process of rheumatoid arthritis.

From the clinical trials it is concluded that the test offers the advantage of considerable specificity, as 91·5% of the cases in which positive results were obtained had been diagnosed clinically as of rheumatoid arthritis. Further, 5 out of 13 false-positive results occurred in patients with arthritic disease which might easily have been labelled "rheumatoid arthritis". The author points out that since rheumatoid arthritis is an ill-defined clinical syndrome which merges with various arthritic, peripheral vascular, and other diseases, any test which facilitates the delineation of a single clinical group might be of value in the study of rheumatic disease.

H. Lehmann

1673. **Insulin and E.C.T. in Treatment of Rheumatoid Arthritis. Report on a Pilot Series of Cases**
G. D. Kersley, L. Mandel, M. R. Jeffrey, M. H. L. Desmarais, and E. Bene. *British Medical Journal* [*Brit. med. J.*] **2**, 855–860, Oct. 14, 1950. 16 refs.

Insulin hypoglycaemia provokes the liberation of adrenaline and thereby may stimulate the adrenal cortex It is possible that this also explains the effect of electric convulsion therapy. It was decided to treat two series of cases of rheumatoid arthritis by these two methods.

Forty cases of active rheumatoid arthritis were treated five times weekly for 3 or 4 weeks by induction of hypoglycaemia with insulin. In 22 cases there was marked improvement, and in 10 this was maintained for 6 weeks after completion of treatment. All the patients gained weight, but there was no significant change in the erythrocyte sedimentation rate. In 24 cases the eosinophil count fell 4½ hours after maximal hypoglycaemia, but there was no apparent correlation between the degree of hypoglycaemia, eosinopenia, and recovery. Neither was there an apparent correlation between the degree of recovery and the depression of eosinophil count provoked by adrenaline or adrenocorticotrophin.

Of 11 patients treated by electric convulsion therapy, an average of five shocks being given, 3 were markedly improved.

It is stressed that further control and follow-up is needed before results of these two forms of treatment can be assessed. *D. P. Nicholson*

Neurology

1674. **Heredopathia Atactica Polyneuritiformis**
H. REESE and J. BARETA. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] **9**, 385–395, 1950. 8 figs., 12 refs.

The case is reported of a 25-year-old male who complained of progressive night blindness from the age of 18. His parents were first cousins, but they and the patient's 4 brothers were all free from disease. The patient had small irregular pupils, slight nystagmus, advanced retinitis pigmentosa, constricted visual fields, intention tremors, hyporeflexia, and anomalous bony development of hands and feet. When he was examined by the authors he was 37 and complained then, in addition to the other symptoms, of inability to walk without support, bilateral deafness, and progressive failure of vision. He was found to have pronounced muscular atrophy with functional disability increasing distally to paralysis in the lower limbs, including the pelvic girdle. He walked with the aid of crutches and by forward hip-swinging of the legs. Sensations of touch, pain, and temperature were preserved, but proprioceptive sense was greatly impaired. Handwriting was rendered difficult on account of fatigue tremors. The cerebrospinal fluid contained 185 mg. of protein per 100 ml. Biopsy of the long peroneal muscle showed atrophic, reddish muscle substance.

During the 13 days he was in hospital he became confused and dyspnoeic. Post-mortem findings included moderate demyelination of the posterior columns, a decrease in the number of anterior horn cells, and interstitial neuritis, with disappearance of individual nerve fibres and replacement by concentric layering of connective tissue in onion-bulb fashion. Between the separated fibres lay a metachromatic substance which, when the tissues were incubated with hyaluronidase, decreased almost to the point of disappearing. Degeneration of axons and a slowly progressive demyelination beginning distally and progressing proximally were thought to be the result of newly formed collagenous tissue enveloping and impinging upon nerve structures.

This is believed to be an instance of Refsum's (1946) heredopathia atactica polyneuritiformis. Clinically, it was a complicated syndrome of familial progressive interstitial hypertrophic polyneuritis of the Déjérine–Sottas variety. *W. H. McMenemey*

1675. **Precentral Motor Cortical Ablation in Experimental Epilepsy in the Monkey**
B. L. PACELLA, M. A. KENNARD, L. M. KOPELOFF, J. G. CHUSID, and N. KOPELOFF. *Journal of Neurosurgery* [*J. Neurosurg.*] **7**, 390–397, Sept., 1950. 8 figs., 3 refs.

The authors have studied the effect of cortical ablation on artificially induced epilepsy in monkeys. Seizures were induced by the application of alumina cream to the cortex or ablation site, or by injection of the same substance into the brain. Operation was carried out under pentobarbitone anaesthesia, the required area of cortex being removed by suction and vessels coagulated or closed with clips. Post-mortem examination showed residual areas of grey matter in all areas of ablation.

In one group of 11 animals, cortical ablation was carried out 3 to 6 months before the application of alumina cream, the sites of ablation and application being varied in each case. Seizures developed in 9 of the animals in this series and became bilateral in 7. The 2 animals that did not develop fits were those which had had the largest cortical excisions in areas 4 and 6. Electroencephalographic findings ran parallel with the clinical results, and no abnormality developed in the 2 animals free of fits.

In another group of animals fits were induced and the effect of subsequent cortical ablation tested. In 2 animals the cortex underlying the treated site was excised (areas 4 and 6 in both cases); in one animal treated over area 4 a partial removal of area 6 was carried out. These removals did not stop attacks, but caused a temporary diminution of electroencephalographic abnormality and inhibition of attacks in 2 cases for 7 months and one year respectively. In one control animal removal of cortex under an application of "inactive" zinc oxide did not produce any change. *E. B. C. Hughes*

1676. **Testosterone in Progressive Pseudohypertrophic Muscular Dystrophy**
M. A. PERLSTEIN and H. GUTTERMAN. *Journal of Pediatrics* [*J. Pediat.*] **37**, 743–749, Nov., 1950. 12 refs.

Eleven young male patients with progressive pseudohypertrophic muscular dystrophy received methyl testosterone in amounts sufficient to promote the appearance of secondary sex characters. Objective evidence (dynamometer studies and throwing ability) failed to reveal sustained clinical improvement in any case. Subjectively most patients felt better. In 2 cases an exacerbation of symptoms was recorded, and in one case weakness increased when the therapy was suspended.—[Authors' summary.]

ELECTROENCEPHALOGRAPHY

1677. **Electroencephalography in Cerebral Palsy**
R. B. AIRD and P. COHEN. *Journal of Pediatrics* [*J. Pediat.*] **37**, 448–454, Oct., 1950. 6 refs.

The group of 187 children with cerebral palsy studied included 128 with spastic features, 53 with athetoid movements, and 6 with disease of unspecified type; all were between 1 year and 21 years of age. Of the spastic patients 85% had an abnormal electroencephalogram (EEG), 62% being focally abnormal; the corresponding figures for the athetoid cases were 60 and 32%.

[The tracings in 2% and 8% of cases respectively were considered borderline; if, as is likely, a high proportion of the patients were in the first decade of life, this implies an unusually confident assessment of these difficult tracings.]

In cases with a known cause for the palsy the likelihood of an abnormal record was high; for example, the record was abnormal in 98% of the spastic cases with a history of injury or infection. When the cases were classified as mild, moderate, or severe, an abnormal EEG was commoner in spastic cases in each group. No correlation could be found between intelligence, ranging from superior to idiot, and the EEG findings. A history of convulsions did not seem to increase the probability of abnormality of the EEG unless the fits were severe.

The authors consider the investigation of value in obtaining a more complete understanding of the patient's condition, but doubt its usefulness in differentiating between spastic and athetoid states. *W. A. Cobb*

1678. **Changes in the Neurological and the Electroencephalographic Picture after Electric Injury.** (Динамика неврологических симптомов и биотоков мозга у больных с электротравмой)
L. I. Aleksandrova and L. G. Makarova. Невропатология и Психиатрия (*Neuropat. Psikhiat.*] **19**, No. 4, 17–22, 1950. 5 figs.

The clinical picture in 5 patients suffering from electric trauma varied considerably, but the electroencephalographic (EEG) findings proved to be a useful guide to the severity of the condition. The main EEG changes were: (1) the disorganization or complete disappearance of the alpha rhythm; (2) a considerable reduction in the amplitude of the action potentials; (3) the presence of spikes in some of the tracings; (4) the presence of regular and irregular slow pathological waves; (5) the visibility of the cardiac rhythm in the EEG; and (6) the appearance of asymmetry between the two hemispheres and homonymous areas. *L. Crome*

1679. **Electroencephalographic Studies of Treatment of Schizophrenia by Electric Convulsion Therapy.** (Электроэнцефалографические исследования при лечении шизофрении электрошоком)
S. A. Chugunov and J. S. Nikolaev. Невропатология и Психиатрия [*Neuropat. Psikhiat.*] **19**, No. 5, 59–64, Sept.–Oct., 1950. 3 figs.

The authors describe their investigations on the changes in electroencephalographic (EEG) patterns resulting from a course of electric convulsion therapy (E.C.T.) in 7 cases of schizophrenia. E.C.T. was given with an alternating current of 100 to 115 volts for 0·05 to 0·8 second [frequency is not recorded]. The convulsions lasted for 18 to 25 seconds, and were followed by stupor for up to half an hour and by retrograde amnesia. EEG records were taken from the occipital, frontal, and parietal regions on both sides.

The pattern before the convulsion was characterized chiefly by irregular α waves, interrupted by β waves of high frequency and of varying amplitude. E.C.T. abolished α waves; in many cases they were replaced by high β waves. In addition, slow waves of 2 to 5 a second and of high voltage (80 to 120 μV) with pointed summits appeared, together with " spike " oscillations of 200 to 250 μV. Groups of waves with frequencies of up to 60 per second were also observed.

After continued treatment (that is, after 10 or more sessions) the α waves returned, but they were irregular both in rhythm and amplitude.

The clinical results varied considerably in these cases; in some cases the condition improved, but in others it became so much worse that treatment had to be suspended. The authors consider that E.C.T. should be confined to cases in which the electroencephalogram is relatively stable and the clinical features indicate retardation of psychological processes. They emphasize the need for caution in the employment of this treatment, and the possibility of serious damage to the brain by the induction of severe convulsions.

[E.C.T. appears to be still widely employed in the U.S.S.R. in the treatment of schizophrenia.]
L. Firman Edwards

1680. **Specific Changes in Cortical Electrical Activity in Schizophrenia.** (К вопросу о специфических изменениях мозговой электроактивности при шизофрении)
F. V. Bassin and A. L. Fedorova. Невропатология и Психиатрия [*Nevropat. Psikhiat.*] **19**, No. 5, 64–70' Sept.–Oct., 1950. 4 figs.

The alleged similarity of cortical disturbances lying at the root of schizophrenia and the epileptic syndromes has not been confirmed by recent researches. Gigishvili and Zurabashvili have advanced the hypothesis that the basic electroencephalographic (EEG) change in schizophrenia (in their opinion pathognomonic of that disease) is an inco-ordination of the EEG records taken simultaneously from the corresponding zones of the two hemispheres. They hold that this lack of co-ordination explains the psychological phenomena characteristic of schizophrenia.

The authors of this article contest the above view, holding that " such an assumption of a direct relation between EEG findings and psychological behaviour is unwarranted " and that the phenomenon of inco-ordination is neither characteristic of all schizophrenics nor peculiar to this class of patient. They give examples both of records of cases of schizophrenia with symmetrical wave patterns, and of asymmetrical patterns in non-schizophrenic conditions, including epilepsy, electrical trauma, and cerebral contusion. They show that in 6 out of 18 cases of schizophrenia inco-ordination was not observed, while 14 out of 17 controls showed this phenomenon.

While denying that this sign is pathognomonic of schizophrenia, the authors emphasize its importance as being linked with certain phases in the development of pathological lesions in the brain. It appears to be found more often in acute and subacute stages than in the residual phase, and more often during the development or subsidence of complications than at their height or in stabilized cerebral injury. They suggest that " inco-ordination of bioelectric rhythm is indicative of unstable

or passing phases in which there exists a disturbance of relations between the various cerebral zones, yet an absence of the conditions which favour the development of more serious pathological EEG signs ".

L. Firman-Edwards

1681. **Electrocorticography and the Surgical Treatment of Focal Epilepsy.** (L'électrocorticogramme et le traitement chirurgical de l'épilepsie focale)
L. Ectors and J. Achslogh. *Bruxelles-Médical* [*Brux.-méd.*] **30**, 1999–2015, Sept. 24, 1950. 7 figs., 3 refs.

CENTRAL NERVOUS SYSTEM

1682. **Electromyographic Study of Disturbances of Deep Sensibility.** (Étude électromyographique des troubles de la sensibilité profonde)
I. Lesny, B. Drechsler, and K. Obrda. *Revue Neurologique* [*Rev. neurol.*] **83**, 192–197, Sept., 1950. 4 figs., 7 refs.

This paper describes investigations with the electromyograph (EMG) in patients with posterior root or horn lesions. These patients included 17 who had had a posterior root section during operation for herniated intervertebral disk in the lumbar region and 23 who were suffering from a neurological disorder (19 with tabes, 3 with subacute combined degeneration of the cord, and 1 with diabetic neuropathy). In all the patients the disturbances were limited clinically to sensory deficit. The EMG was recorded from muscles corresponding to the dermatome of the affected sensory root or horn.

In all except one patient with neurological disease [unspecified] the EMG was abnormal and showed marked diminution of frequency (below 28 c.p.s.) in the motor units. In almost all the cases of posterior root section and in 8 of those of neurological disease occurred the " single oscillations " regarded as characteristic of denervated muscle or motor nerve palsy. Sometimes these were reduplicated to give the " doublets " described by Lefèbvre and by Denny-Brown. The authors conclude that it is not only the " motor unit " of Sherrington which is responsible for the EMG activity, but the whole of the spinal reflex arc. They suggest that the intersynaptic potentials between posterior and anterior horn cells may be important factors in muscular electrical activity.

J. B. Stanton

1683. **Multiple Sclerosis: a Correlation of its Incidence with Dietary Fat**
R. L. Swank. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **220**, 421–430, Oct., 1950. 3 figs., 17 refs.

The author, who is Assistant Professor of Experimental Neurology at McGill University, Montreal, states that it is generally agreed that disseminated sclerosis has a much greater incidence in cold and temperate climates than in warmer and subtropical areas. A chart of the average daily fat intake of inhabitants of various countries shows that this is inversely proportional to the temperature, so that the incidence of disseminated sclerosis would appear to be higher in those countries in which a high-fat diet is taken.

Approaching the problem from another angle, the author correlates the annual incidence of this disease (calculated from hospital admissions and insurance figures) in Norway, Denmark, and Holland between 1930 and 1948 with the average daily calorie intake and the amount of fat in the diet. From this it appears that in each of the 3 countries there was a marked fall in the incidence of disseminated sclerosis during the early 1930's during a time when calorie intake had fallen owing to economic depression, the reduction being due almost entirely to reduction in fat intake. With the return of comparative prosperity more food was eaten, especially fat, and in each country there was a substantial increase in incidence of disseminated sclerosis. During the war years, coinciding with a marked lowering of the dietary fat, there was again a reduction in the number of diagnosed cases of the disease, only to be followed later by a rise after the war when more fat became available for food. The hospitals from which statistics were obtained were not materially affected by the war, and drew their patients from the same geographical areas as before. There was nothing to suggest any change in diagnostic criteria.

The author also reports that among 5,000 Jewish refugees arriving in Switzerland from Vienna between 1942 and 1949 and thus obtaining a higher fat intake, at least 8 cases of disseminated sclerosis developed. This incidence is double the highest recorded for Switzerland and more than treble that in Denmark. Similarly among 10,000 Danish prisoners repatriated from Germany 5 developed disseminated sclerosis after being fed on a full diet with high fat content, whereas no case of this disease had developed while they were kept in German camps on low diets. Figures showing the geographical variation of the disease within various countries are given, and appear to indicate a higher incidence among the rural population; and the fact that neurologists who examined groups of prisoners of war frequently recorded neurological complications, but never disseminated sclerosis, is also quoted. It is suggested that these observations indicate that a high fat diet may possibly play an aetiological role in disseminated sclerosis.

M. H. Pappworth

1684. **Biochemical Studies in Multiple Sclerosis**
H. H. Jones, H. H. Jones, Jr., and L. D. Bunch. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 831–840, Oct., 1950. 5 figs., 42 refs.

Clinical observations and isolated biochemical findings suggested to the authors that disseminated sclerosis may be associated with a disorder of carbohydrate metabolism. At the Snyder Research Foundation, Winfield, Kansas, they therefore carried out biochemical investigations on 40 patients with disseminated sclerosis in relapse, 38 patients in remission, and 30 comparable healthy controls. Blood glucose, pyruvic acid, and lactic acid levels were determined before, and at hourly intervals after, a standard oral dose of glucose given under carefully controlled conditions. A constant and statistically

significant increase in the blood pyruvic acid level relative to that of lactic acid was found in the cases in relapse. The blood and urine content of various other metabolites was studied without any findings of like significance. It is suggested that disseminated sclerosis is associated with a specific defect in carbohydrate metabolism, which is probably an interference with the final stages of the oxidation of glucose in the tissues.

[This is a careful study which appears to present a field for further research.] *T. A. A. Hunter*

1685. **The Origin of Reflex Contractures and the Reversal of Central Contractures in the Light of Experiments on Decerebrate Animals.** (Возникновение рефлекторных и извращение центральных контрактур в свете экспериментов на децеребрированных животных)
S. I. Frankstein. Невроматология и Психиатрия [*Neuropat. Psikhiat.*] **19**, No. 4, 51–54, 1950.

Decerebrate rigidity was produced in cats by division of the brain-stem between the superior and the inferior colliculi. At the same time an inflammatory lesion in one of the animal's feet was induced by injection of turpentine. The ensuing changes in the state of decerebrate rigidity and spontaneous reflexes could then be studied. It was found that the presence of such an inflammatory focus led at first to an inhibition of extensor tone and later to development of flexion. This alteration of reflexes was not confined to the injured limb but extended also to the sound ones in accordance with Sherrington's principle of reciprocal limb innervation. The changes in the reflexes persisted after full healing of the injured foot. In other animals both the injured foot and the opposite limb were splinted in plaster-of-Paris; 3 to 5 days after the removal of the bandages the animals could use their injured feet freely. In spite of this, decerebration led to a reversed state of rigidity.

These observations in cats provide an analogy to the well-known phenomenon seen in paraplegic patients, in which rigidity in extension is sometimes succeeded by rigidity in flexion after some injury to a limb or on development of an inflammatory focus such as cystitis. It seems that peripheral injury, or its trace, can produce a state of reflex irritation in the central nervous system. If the latter is intact, this altered state is often hidden, or manifests itself only in some temporary disturbance of locomotion. If, however, the ability of the central nervous system to compensate is inhibited by trauma, disease, or, as in the above experiments, by decerebration, then the tonic reflexes in the limbs are more permanently altered. *L. Crome*

1686. **The Reflection of Trauma of the Spinal Cord on Visceral Function.** (Отражение травмы спинного моега на функциях внутренних органов)
K. M. Freidin. Невромателогия и психиатрия [*Neuropat. Psikhiat.*] **19**, No. 4, 34–38, 1950. 3 refs.

A study of the function of the heart, the digestive organs, and the urinary system, and of some aspects of metabolism, was undertaken in 300 patients suffering from various injuries of the spinal cord. The results, which are reported fully, indicated significant changes in all of the above visceral functions. *L. Crome*

1687. **The Problem of Paraplegic Flexion Contractures.** (К вопросу о механизме сгибательных параплегических контрактур)
I. B. Wainstock. Невроиатологя и Психиатрия [*Neuropat. Psikhiat.*] **19**, No. 4, 48–51, 1950.

Clinical observations and experimental data are cited in support of the view that flexion contractures in paraplegic patients are initiated by constant mechanical or inflammatory irritation of the peripheral sensory neurons. These contractures can be temporarily inhibited by nerve-root block with procaine. The operative sensory impulses need not be derived necessarily from the paralysed legs; similar contractures may be produced in them by noxious stimuli derived from the non-paralysed upper limbs. *L. Crome*

BRAIN

1688. **Delayed Effects of Seemingly Minor Head Injuries.**
B. Schlesinger. *Diseases of the Nervous System* [*Dis. nerv. Syst.*] **65**, 259–267, Sept., 1950. 2 figs., 16 refs.

This paper is concerned with a group of cases in which serious neurological disorders developed, after a latent interval, as a result of relatively mild injuries to the head. The author seeks to prove that these sequelae in his series resulted from injury to an artery, followed by spreading thromboses. Such thromboses are stated to be distinguishable from massive surface haemorrhages because, in spite of the development of focal neurological signs, the general condition of the patient does not deteriorate. *G. F. Rowbotham*

1689. **A Case of Association of the Laurence–Moon–Biedl Syndrome with Persistent Cavum Septi Pellucidi.** (Sobre un caso de asociacion de sindrome de Laurence–Moon–Biedl con cavum septi pellucidi)
A. J. Campo, R. Carrea, E. O. Correa, and —. Araujo. *Archivos Argentinos de Pediatria* [*Arch. argent. Pediat.*] **21**, 89–104, Aug., 1950. 4 figs., 40 refs.

The authors discuss the diagnosis and pathogenesis of the Laurence–Moon–Biedl syndrome and persistence of the cavity of the septum lucidum. A good review and a bibliography of the current literature are given. Operative procedures for the treatment of closed dilatations of the fifth and sixth ventricles are discussed.

An account is given of a 9-month-old male baby with the Laurence–Moon–Biedl syndrome associated with a progressive and intermittent hydrocephalus. There was generalized hypotonia, and reflexes were normal. Ophthalmoscopic examination showed retinitis pigmentosa. On each foot there were six toes. The sixth finger of each hand had previously been removed surgically. The father, grandfather, and paternal uncles were obese and all had polydactyly of the hands and feet. The Wassermann reaction was positive in both mother and child.

Pneumoencephalography showed evidence of a non-communicating cavum septi pellucidi, or possibly a tumour of the corpus callosum. During ventriculography the wall of the cavum septi pellucidi was broken, resulting in immediate relief of the stenosis of the interventricular foramina and permanent relief of the hydrocephalus. Rapid psychomotor movements followed this relief. The mental deficiency and changes in the electroencephalogram were attributed to compression atrophy of the cerebrum. A short time after the operation the child's mental state had improved considerably.

René Méndez

1690. **Cerebral Apoplexy Considered in Relation to the Pathogenesis of Spontaneous Haemorrhage and of Thrombosis.** (L'apoplessia cerebrale nel quadro della patogenesi angiopatica della emorragia spontanea e della trombosi)

P. MENEGHINI and A. PAVERO. *Archivio "E. Maragliano" di Patologia e Clinica* [*Arch. "E. Maragliano" Pat. Clin.*] **5**, 869–878, Sept.–Oct., 1950. 1 fig., 28 refs.

Details are given of the case histories of 13 patients of both sexes, aged 46 to 72 years, 5 of whom had had recent cerebral haemorrhage, 4 recent cerebral thrombosis, one a "cerebral claudication", and 3 longer-standing hemiplegia. The last 3 had had their lesions for 30 to 180 days, the other 10 for 1 to 17 days. In all cases and in an unspecified number [? one], of the normal control patients the coagulation time of the blood was measured by two methods (Howell and Quick) and the plasma heparin level estimated by the toluidin-blue method. In certain cases post-mortem histological studies of the affected areas were made. In all affected patients the coagulation time was diminished and the plasma heparin level decreased. It is suggested that cerebral vascular catastrophe follows upon the development of these blood changes in the presence of predisposing local vascular pathology.

James D. P. Graham

1691. **Latent Aphasia. Diagnosis in Cerebral Arteriosclerosis by a Vocabulary Test.** (L'aphasie latente, son diagnostic dans l'artériosclérose cérébrale au moyen d'un test de vocabulaire)

J. DELAY, P. PICHOT, R. DURSAP, and J. PERSE. *Revue Neurologique* [*Rev. neurol.*] **83**, 180–191, Sept., 1950. 6 figs., 3 refs.

The authors have performed psychometric tests on two groups of patients, of comparable educational and social levels, suffering from dementia—27 patients in whom the condition was diagnosed clinically as arteriopathic in origin and 25 in whom it was regarded as senile in origin. None of the patients suffered from aphasia demonstrable clinically, and none was too grossly demented to co-operate. With Raven's progressive matrices both groups showed a marked and statistically comparable intellectual deterioriation, which was confirmed by Kohs's block-design and similar tests. In vocabulary tests, however, the arteriopathic group had an average score which statistical treatment showed to be significantly below that for senile dements, and a similar, but statistically unanalysable, inferiority on the part of the arteriopaths was manifest in Thurstone's factor-W test. The authors suggest that the explanation of this unusually low score in vocabulary tests in the arteriopathic group, which was not found in other types of mental deterioration, must lie in the presence of a latent aphasia, and they indicate the possible value of this in differentiating arteriopathic from other dementias.

J. B. Stanton

1692. **A Lethargic Form of Encephalitis with Psychotic Manifestations.** (Сонная форма энцефалита с нарушениями психики)

F. M. LISITSA. Невропатология и Психиатрия (*Neuropat. Psikhiat.*] **19**, No. 4, 23–27, 1950. 3 figs.

Three cases of lethargic encephalitis occurred in Tadjikistan between January and March, 1948. The onset in each case was sudden, and the condition was characterized by torpor, somnolence lasting 2 to 3 weeks, and akinesia. Transient hemiplegia developed in one of the cases. After the termination of the acute period, episodes of euphoria and delirium occurred in a few instances. The after-effects consisted of slight mental fatiguability and mild disturbance of memory. No Parkinsonism developed in the course of the following 2 years. Tadjikistan was completely spared by the pandemic of encephalitis lethargica of 1919–21.

L. Crome

1693. **Psychical Paralysis of Vision (Balint) during the Development of a Leuco-encephalitis of Baló Type.** (Paralysie psychique du regard de Balint au cours de l'évolution d'une leucoencéphalite type Baló)

H. HECAEN, J. DE AJURIAGUERRA, L. ROUGUÈS, M. DAVID, and M. B. DELL. *Revue Neurologique* [*Rev. neurol.*] **83**, 81–104, Aug., 1950. 8 figs., 18 refs.

Translating Balint's *Seelenlähmung des Schauens* as *paralysie psychique du regard*, the authors discuss at length a case of the leuco-encephalitis periaxialis concentrica of Baló. The pathological discussion is brief and, after the long clinical account, attention is devoted first to the re-interpretation in French of what Balint said in German and then to an analytical comparison of the authors' and Balint's views. The case described was that of a man of 33 who suddenly became comatose for a period of 48 hours. He emerged with a right hemiparesis and an alexia. Five months later a steady deterioration set in, characterized initially by aphasia, astereognosis, and defective spatial localization.

He was first examined by the authors 6 months after the onset of his illness, by which time he could not speak, write, or read, and apraxia was prominent. The hemiplegia was still present together with some signs of cortical sensory affection. Sensory testing was naturally rather difficult. What really aroused interest, however, was the fixation of his gaze and his apparent associated impairment of vision. Briefly, his oculomotor disturbance was as follows: (1) Although he could alter the direction of his gaze when instructed to look either to left or to right, he was quite unable to carry out following movements. (2) If an object were moved from the point of central fixation, he was unable to see it, and such

action was often followed by a rather aimless wandering movement of the eyes. (3) Once an object was brought into the position of central vision, his eyes remained fixed upon it. Death occurred 2 months later and 2 days after exploration. Necropsy revealed a very diffuse demyelinating affection of the cerebral white matter. The cerebral peduncles and pons were pale but not demyelinated. [Nothing is said about the cord.] The optic chiasma and its immediate connexions were normal.

In discussing the case, the authors stress chiefly the gaze palsy. The term " psychic " was justified by Balint by his belief that, given circumstances in which the higher psychical functions were not called upon, oculomotor function remained normal. Two other connected features are discussed: (1) optic ataxia, the inability to carry out co-ordinated movements depending upon visual direction alone; and (2) an attention defect, the patient's inability to give attention to any visual stimulus immediateiy outside his point of central fixation.

The authors reject Balint's explanation of this gaze palsy—namely, a visual attention defect related to the psycho-visual areas. Instead, they suggest that frontal oculomotor centres normally exercise a controlling influence over the purely visual reactions of the occipital centres. In bilateral cerebral lesions the integrated function of these centres is disturbed with resultant " optic ataxia ". This theory is, however, qualified to some extent by the admission that the disturbance of visual sensory function may also play a part. The possibility of accurate localization of the lesion producing this gaze palsy is then considered, but this leads to the conclusion that the syndrome probably develops only in cases of extensive structural disorganization.

[This interesting paper is notable both for the characteristic, detailed clinical account and the extensive discussion (10 pages). It is perhaps unkind to mention that the graceful flow of language tends to obscure the fact that its message is simply that a very extensive brain lesion produced, among many other symptoms and signs, a gaze palsy similar to that sometimes seen in Parkinsonism, but possibly accentuated here by a considerable visual impairment.] *L. A. Liversedge*

1694. **Medulloblastoma**

N. RINGERTZ and J. H. TOLA. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] **9**, 354–372, Oct., 1950. 12 figs., 29 refs.

In a series of 1,571 cases of glioma there were 111 instances of medulloblastoma, in 89 of which the growth occurred posteriorly in the midline of the cerebellum, in 6 anteriorly, and in 16 laterally. The tumours which lay anteriorly were connected with the anterior medullary velum, but did not extend behind the fastigium; they sometimes protruded into the anterior part of the 4th ventricle, but the main part always grew forward covering the lamina quadrigemina, invading the anterior vermis and pineal region, and sometimes herniating into the 3rd ventricle through its roof. At operation such growths may occasionally be confused with pinealomata or even meningiomata, for infiltration of cerebrum and subarachnoid spread over cerebellum and posterior ventral parts of cerebrum has been noted. The occurrence of tumours in this anterior location suggests that the proliferation of the embryonal cells may take place in the anterior medullary velum. Of the tumours which lay laterally, 13 were intracerebellar and 3 were in the cerebello-pontine angle, their origin being thought to be due possibly to a lateral medullary velum at the tip of the recess; Waltman, Kernohan, and Adson have described eight instances of ependymoma and two of astrocytoma at this site.

The mode of origin of the midcerebellar tumours is regarded as obscure, with either the external granular layer or an embryonal residue in the medullary velum being considered as a probable source. Attention is drawn to the small lymphocyte-like nuclei with dense structureless chromatin scattered among the medulloblasts; this cell is probably a necrobiotic phase of the medulloblast, for it is found most commonly in areas of necrosis. Unipolar and bipolar spongioblasts were found both in the central part of the tumour and also in the arachnoid infiltrations and are evidence, the authors believe, of cell differentiation. Astrocytes, on the other hand, seen only in the zone of infiltration, are the result of inclusion; neuroblasts were not recognized for certain in the substance of the tumour. It appears that in practically all medulloblastomata a large part of the solid tumour tissue consists of massive pia-arachnoid infiltrates which start in the depth of the cerebellar sulci and become coalescent by destroying the invaded gyri between them.

The average duration before operation was 4·4 months, the shortest period being one week, the longest 72 months. The average period of survival after operation was 16·4 months, the longest being 64 months. The over-all mortality was 34%, but it was only 21% in the 42 cases where the tumours were smaller and radical extirpation was carried out,. *W. H. McMenemey*

1695. **Primary Diffuse Tumors of the Meninges (So-called Meningeal Meningiomatosis)**

B. K. BLACK and J. W. KERNOHAN. *Cancer* [*Cancer*] **3**, 805–819, Sept., 1950. 17 figs., 27 refs.

Four cases of diffuse cellular tumours of the meninges, believed to be of primary meningeal origin, all occurring in children or young adults, are described. The figures depict interesting examples of invasion of the brain or of the cord by these unusual growths. *R. A. Willis*

1696. **Meningiomas of the Sphenoidal Ridge: a Clinicopathologic Study**

E. D. HORNING and J. W. KERNOHAN. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] **9**, 373–384, Oct., 1950. 5 figs., 9 refs.

A study was made of 64 cases of meningioma of the sphenoidal ridge (the third most common anatomical location, according to Cushing and Eisenhardt); 48 of the tumours were found to be, in the classification of Bailey and Bucy, meningotheliomatous, 6 psammomatous, and 6 fibroblastic. Two were of mixed type and

2 could not be classified. The origin in 29 was from the inner third of the ridge, causing headache and visual failure; proptosis was noted in 4 patients, personality changes in 5, and anosmia in 3. In 15 the origin was from the middle third of the ridge, but the symptoms were inconstant; personality changes, however, occurred in 8 patients, anosmia in 5, and proptosis in 6. There were 20 tumours arising from the outer third of the ridge (8 being tumours *en plaque*); proptosis occurred in 13 instances.

The commonest complaint was visual failure (32 patients). Headache was noted by 37 patients, but only 5 gave it as their chief complaint. Proptosis was the principal symptom in 7, but was complained of by 15 and noted in 20. Although the age at which the patients came under observation ranged from 18 to 62 years, no fewer than 40% of them were in the fifth decade. The histories ranged from 4 months to 20 years, with an average of 4·7 years. Trauma was associated with the onset of the symptoms in only 3 of these patients, in contrast to Cushing's and Eisenhardt's 12 in a series of 53 cases. Radiographs failed to help in the diagnosis in only 11 of the series. *W. H. McMenemey*

1697. **A Special Type of Extrapyramidal Syndrome with Unusual Involuntary Movements, a Variable Psychical Component, and a Rapidly Fatal Course.** (Sur un type nosologique spécial de syndrome extrapyramidal avec mouvements involontaires particuliers, composante psychique variable, d'évolution rapidement mortelle. Étude anatomo-clinique)

R. GARCIN, I. BERTRAND, L. VAN BOGAERT, J. GRUNER, and S. BRION. *Revue Neurologique* [*Rev. neurol.*] **83**, 161–179, Sept., 1950. 8 figs., 1 ref.

The authors describe 3 cases of a clinical syndrome characterized by: (1) onset after 50 years of age; (2) extrapyramidal syndrome accompanied by atypical involuntary movements; (3) variable psychical changes; and (4) a progressive course, fatal after a few months. In all 3 cases the onset was fairly sudden, with dysarthria, mental changes, and involuntary movements of the lips or of one upper limb, soon to be followed by disturbances of equilibrium and generalized involuntary movements. These were of an unusual type; voluntary movement of one limb, mental concentration, or, in the later stages, any cutaneous stimulus released wide involuntary movements of the other limbs. Tone was variably affected, and voluntary movement was opposed by spasm of antagonists. Myoclonic jerks were common, and rhythmic tremors and choreiform movements also occurred. There was visuo-spatial disorganization in one case. The mental changes were those of progressive intellectual enfeeblement and memory loss, with anxiety or lability of mood. Physical examination revealed, apart from the dysarthria and extrapyramidal signs, no evidence of infection or raised intracranial pressure. There were nystagmus, oculomotor disturbances, pupillary inequality, tremors of lips and tongue, with gross disturbance of cortical sensation in the limbs and, in one case only, bilateral pyramidal deficit. General medical examination and laboratory tests revealed no significant abnormality. All the patients died in coma with a decerebrate state and some degree of hyperthermia.

Post-mortem examination in 2 of the cases showed a diffuse, non-specific degeneration of nerve cells with variable glial reaction, most marked in the central and frontal cortex, the thalamus, putamen, and subthalamus. There was no evidence of inflammation, and the areas of maximum degeneration did not correspond to any circumscribed vascular territory. Other findings were unremarkable except for mild periportal hepatic degeneration in one case.

The authors consider the nosologic relationship of this unusual neurological syndrome of the presenium. They do not regard it as conforming to the Jakob–Creutzfeld syndrome as originally described, and tentatively suggest its affinity with the syndrome described by Alajouanine and van Bogaert (*Rev. Neurol.*, 1950, **82**, 21).

J. B. Stanton

1698. **Status Marmoratus: a Form of Cerebral Palsy following either Birth Injury or Inflammation of the Central Nervous System**

N. MALAMUD. *Journal of Pediatrics* [*J. Pediat.*] **37**, 610–619, Oct., 1950. 5 figs., 9 refs.

The author summarizes the clinical manifestations of status marmoratus as: spasticity, bilateral choreoathetosis, mental retardation, and epileptic seizures. The characteristic marbled appearance of the basal nuclei is seen microscopically to be due to fine medullated nerves separating the nuclear masses, with dispersion of the latter and an increase in glial elements.

Details of the birth and early history and of the permanent clinical signs and symptoms in 15 cases are given. They are divided into two groups, one of 12 attributed to birth injury, and one of 3 due to post-natal infection. Details of the pathological findings are given and conform to the usual pattern, though in many cases more diffuse lesions are described. The putamen was bilaterally and severely affected in all cases, as was the globus pallidus to a lesser extent. The caudate nucleus was affected bilaterally in 11 cases, unilaterally in 1, and not at all in 3. Where the involvement was not bilateral no athetoid movements had occurred. The thalamus was severely and bilaterally involved in 13 cases, mildly in 1 case, and not at all in one. The cortex was affected in 8 cases. Idiocy was present whenever either the cortex or thalamus was involved. The other basal nuclei, the substantia nigra, the mamillary bodies, and the cerebellum were less constantly involved.

It is concluded that this is not a single disease entity, but the result of varying pathological processes. The incidence of birth injury in the present series is high. The localization of the lesions predominately to the area drained by the Galenic system of veins suggests the possibility of thrombosis of these veins being of aetiological significance. One such case is described.

[It is not clear how this theory can explain cases due to infection, nor is it clear why the last case is included in the infective group. As is conceded by the author, on the evidence given it might equally well fall in the group due to birth injury.] *H. G. Farquhar*

Psychiatry

1699. **A Neuro-physiological Study of Acute Infective Psychoses.** (Опыт нейрофизиологического изучения острых инфекционных психозов)
L. A. Balanov, M. I. Sandomirsky, N. N. Traugott, and A. S. Tchistovitch. Невропатология и Психиатрия [*Neuropat. Psikhiat.*] **19**, No. 4, 65–70, 1950. 1 fig.

Seven patients with acute infective psychoses were studied by neuro-physiological methods. The formation of new conditioned reflexes in them was found to be almost impossible, and the utilization of old experience was considerably impaired. The activity of the second signalling system was particularly deranged. Such inhibition of the higher cortical activity at times unmasked or exaggerated activity at a more primitive level. This was particularly so in the case of the orientation reflex, in which skin stimulation was found to be consistently more effective than external visual or acoustic stimulation. The changes extended beyond cortical function and involved some of the unconditioned reflexes.

L. Crome

1700. **Study of a Case of Phacomatosis in Tuberous Sclerosis Treated by Topectomy.** (Étude anatomo-clinique et évolutive d'une phakomatose de Bourneville traitée par topectomie)
G. Heuyer, M. Feld, H. Berdet, and J. Martinetti. *Revue Neurologique* [*Rev. neurol.*] **83**, 105–118, Aug., 1950. 6 figs., 16 refs.

A short account of the features of Bourneville's disease is followed by a case report of a girl, aged 11, a mentally defective epileptic with adenoma sebaceum, who was also incontinent, aphasic, and inarticulate. Her gait was ataxic and jerky. The cranial nerves were normal, the limbs were hypotonic, and there was some amyotrophy of the arms. Tendon reflexes were diminished but equal, abdominal reflexes absent, and plantar response extensor. Bilateral claw foot was present. Her behaviour was very surly, aggressive if cornered, and at times requiring restraint. No intracranial calcification was seen on the radiograph. The cerebro-spinal fluid was normal. The Wassermann reaction was negative. Previous encephalography had revealed slight dilatation of the ventricles.

In view of her aggressive behaviour it was decided to carry out prefrontal topectomy. Subsequently her conduct was much quieter and continued so; 6 months later gingivitis occurred (she was taking sodium diphenyl-hydantoinate); 18 months later, however, she developed a paraplegia which became complete over a period of 3 weeks. A new encephalogram showed a rather more pronounced dilatation of the ventricles. Examination of the topectomy material revealed the characteristic large neuronal and glial cells of tuberous sclerosis.

The authors comment on: (1) The mucosal anomalies occurring in this condition (she had also had gingivitis at the age of 7). (2) The effect of topectomy in improving her behaviour: areas 9 and 10 had been ablated with success. (3) The better response of her epilepsy to medication after the operation [but details are not given]. (4) The unusual clinical signs, reminiscent of Friedreich's ataxia developing later into paraplegia in flexion; also the apparent cerebellar atrophy following the prefrontal operation. They suggest the possibility of trans-synaptic degeneration of the cerebellum dependent upon the prefrontal section. (5) The fact that the patient's father had an angioma; a possible aetiological connexion is suggested.

[This is a rather unsatisfactory, speculative paper which needs to be supported by post-mortem evidence. The radiographs purporting to show the relative sizes of the ventricles before and after operation are not themselves of comparable size.] *L. A. Liversedge*

1701. **Excretion of Phenylalanine and Derivatives in Phenylpyruvic Oligophrenia**
G. A. Jervis. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 83–86, Oct., 1950. 20 refs.

The urinary excretion of phenylalanine and its derivatives was studied in 20 patients affected by phenylpyruvic oligophrenia, under varying dietary conditions. The ages of the patients ranged from 2 to 42 years and their intelligence quotients from 5 to 47.

The values of the phenyl compounds are expressed in mg. per g. of total nitrogen in the urine. The output of phenylalanine on normal institutional diet was found to vary between 20 and 50 mg., that of phenylpyruvic acid from 112 to 181 mg., and that of phenyl lactic acid from 41 to 91 mg. There was no conspicuous difference in the output of phenyl compounds from patient to patient; a relative constancy of the ratios of urinary phenyl compounds to total urinary nitrogen suggested that only small differences occur in the degree of metabolic error. No correlation could be established between the degree of mental deficiency and amount of excreted phenyl compounds.

Giving a high- followed by a low-protein diet to one patient showed that the amount of phenyl compounds excreted depends on the amount of protein ingested. However, 2 other patients still excreted phenylalanine and its keto- and hydroxy-acids after 10 days on a protein-free diet, so that not all phenyl compounds are derived from dietary protein.

Ingestion of various amino-acids (glycine, glutamic acid, tyrosine, alanine, and cystine) produced no change in the output of phenyl compounds. The ingestion of 10 g. DL-phenylalanine and of 10 g. phenylpyruvic acid by patients kept on a nitrogen-constant diet increased the excretion of all three phenyl compounds. However, since the ratio of phenylalanine to nitrogen in various

foods does not vary significantly, it is probable that the quality of ingested food does not affect the amount of phenyl compounds excreted per g. of nitrogen.

Amounts of phenylalanine in sweat, determined in 10 patients, were somewhat higher than in normal individuals. Phenylpyruvic acid, not excreted in sweat by normal individuals, was found in values varying from 6 to 56 mg. per 100 ml. Phenyl lactic acid was not found in measurable amounts in the sweat.

[The details of the methods of determination of the phenyl compounds in the urine should be studied in the original.] *Catherine Schöpflin*

1702. **Oligophrenia Phenylpyruvica. II. Constancy of the Metabolic Error**

E. BOREK, A. BRECHER, G. A. JERVIS, and H. WAELSCH. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 86–89, Oct., 1950. 4 refs.

The levels of phenylalanine and its derivatives in serum and cerebrospinal fluid (C.S.F.) were investigated in oligophrenia phenylpyruvica.

Quantitative determinations of the sum of phenylalanine and phenyl lactic acid in serum and of phenylalanine in the C.S.F. were carried out in 18 fasting patients with phenylketonuria. The concentration of phenylalanine varied from 19 to 38 mg. per 100 ml. of serum. The difference between the sum of phenylalanine and phenyl lactic acid on the one hand and phenylalanine alone on the other was very small, showing that only traces of the hydroxy-acid are circulating in the blood. Variations of the values in an individual were significantly smaller than variations from patient to patient, suggesting a characteristic, relatively constant, blood level of phenylalanine for each individual. No correlation could be found between the phenylalanine level in the serum and the degree of mental deficiency. The concentration of phenylalanine in the C.S.F. varied from 6·1 to 8·2 mg. per 100 ml.

The urinary excretion of phenylalanine and its metabolites is secondary to the high blood concentration of this amino-acid. The relative constancy of the level of phenylalanine in serum explains the relative constancy of the ratios of urinary phenyl compounds to urinary nitrogen, since the amount of the urinary output depends on the amount of phenylalanine circulating through the kidney.

To 2 fasting patients with oligophrenia phenylpyruvica and to one control (also a mental defective) 1·6 g. L-phenylalanine was administered intravenously. The phenylalanine rapidly disappeared from the blood into the tissues, but was only slowly released from there, since the content of phenyl derivatives in the urine samples—obtained simultaneously with the blood samples—showed no significant changes during the first 2 hours after administration of phenylalanine.

It is suggested by the authors that the non-utilization of phenylalanine in cases of phenylketonuria leads to the presence of such a high level of this amino-acid in the glomerular filtrate that the tubules are unable to reabsorb it. *Catherine Schöpflin*

1703. **Ulcerative Colitis. A Study of 173 Cases**

J. W. PAULLEY. *Gastroenterology* [*Gastroenterology*] **16**, 566–576, Nov., 1950. 43 refs.

The author describes an investigation of 173 patients with ulcerative colitis. He concludes that the psychological factor is the most important and that other agents, such as allergy and nutritional deficiency, play no part in aetiology. Each patient was interviewed at length in private, and personal history was obtained from the relatives. Certain features of personality were found in almost all. The patients were excessively dependent and under the control of the parents, usually the mother, and were usually described as having been model children. They were never outwardly aggressive, though often querulous; they were very sensitive and tended to brood over real or imagined wrongs and insults. The men were rather effeminate, and fastidiousness and neatness were common in both sexes. Other characteristics were a tendency to self-righteousness, smugness, and false modesty, and a poor sense of humour. They were "chicken-hearted" and much upset by the sight of blood. An important finding was the inability to express emotion adequately. As a group the patients were emotionally immature; maternal dominance and possessiveness served as a predisposing cause of this state. The present study showed that the incidence of colitis in Jews was double the rate to be anticipated. The father of a patient with colitis was generally weak and ineffectual, or tough, unsympathetic, and addicted to alcohol. Events which seemed to precipitate the illness were those which disturbed personal relationships within the family, especially changes which threatened the patient's dependence.

A control group of 98 patients who were undergoing radiotherapy were interviewed. Only 5 of these had a personality pattern close to that outlined above, though 30% showed some traits of emotional immaturity. In psychotherapy for ulcerative colitis the physician should act as a temporary substitute for the mother. A useful measure is to encourage acts of independence. Outpatient treatment is preferable to admission to a general ward. In this series 2 patients, one of whom had been ill for 18 years and the other for 9, were restored to health by treatment of this kind. Psychotherapy proved most successful in young men.

[Everyone interested in this subject will look forward to the publication of the results of psychotherapy in all the cases treated by the author.] *Desmond O'Neill*

1704. **Addiction Liabilities of Morphinan, 6-Methyldihydromorphine and Dihydrocodeinone**

H. F. FRASER and H. ISABELL. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **100**, 128–135, Oct., 1950. 2 figs., 11 refs.

Each of the three substances, morphinan, 6 methyldihydromorphine, and dihydrocodeinone, was found to induce euphoria in former morphine addicts and to relieve symptoms of morphine withdrawal. When the drugs were administered in increasing doses over periods of 30 to 38 days to three groups of 5 former morphine addicts the subjects all developed tolerance and showed

abstinence symptoms on withdrawal. These were most severe in the case of morphinan and least in that of 6-methyldihydromorphine. The final daily dosage of morphinan was 60 mg., of 6-methyldihydromorphine 180 mg., and of dihydrocodeinone 240 mg. It was considered that the best results were given by 6-methyldihydromorphine, which afforded the greatest relief in morphine abstinence and gave rise to the minimal withdrawal symptoms. *V. J. Woolley*

1705. **Intravenous Barbiturate Anaesthesia in Hysterical Syndromes.** (Narcosi barbiturica endovenosa. Modificazioni clinicobiologiche nelle sindromi isteriche)
R. BALBI and A. BARONE. *Acta Neurologica* [*Acta neurol., Napoli*] **5**, 512–545, Sept.–Oct., 1950. 31 refs.

The technique used in these studies was standard. The barbiturates employed for treatment of hysterical syndromes were thiopentone sodium or similar preparations with longer action. The patient was usually examined psychologically in the period of subnarcosis during recovery from complete unconsciousness (defined by the absence of reaction to pressure on the supraorbital nerve).

Eleven cases with varying hysterical manifestations are reported in detail, a total of 15 treatments having been given. Cure was achieved in 4 cases (notable in 2 cases of aphonia and one case of mutism), and marked improvement in one further case. A transitory slight improvement was noted in 4 other cases.

The condition of the patient was assessed by clinical examination, and the levels of potassium, glucose, chloride, calcium, and cholinesterase in the blood were estimated. These biochemical investigations rarely revealed changes outside normal limits. The potassium level usually rose slightly as a result of narcosis and the calcium level tended to fall so that the K/Ca ratio increased in all cases. When values before treatment were abnormal, clinical improvement was accompanied by return of potassium and calcium levels to normal.
Donald Mc Donald

1706. **Effect of Treatment on Excretion of 17-Ketosteroids in Patients with Mental Disease**
M. D. ALTSCHULE and B. H. PARKHURST. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **64**, 516–527, Oct., 1950. 10 figs., 29 refs.

In 69 psychotic or severely neurotic patients the daily urinary excretion of 17-ketosteroids was found to be within normal limits. Treatment with brief psychotherapy (2 cases), insulin therapy (3 cases), and electric shock therapy (9 cases) had a variable effect on the output of 17-ketosteroids. The authors claim, however, that in those cases studied over a long period (10 to 80 days) and in which marked improvement occurred, a "lowering of the average output of 17-ketosteroids occurred in every instance".

[This conclusion is not entirely borne out by the data presented. In 2 cases the authors have to resort to the assumption that the improvement diagnosed by the clinical staff was an error of judgment. They try to support their conclusion by a re-evaluation of the investigations of Ashby on patients in England (*J. ment. Sci.*, 1949, **95**, 275), asserting that in two-thirds of these cases there was a late fall in the output of 17-ketosteroids. They also imply that this would have been observed more consistently but for the initial presence of "severe malnutrition"—an assumption for which there is no basis in Ashby's paper.] *F. K. Taylor*

1707. **A Comparison of Desoxyephedrine (Methedrine), and Electroshock in the Treatment of Depression**
A. B. MONRO and H. CONITZER. *The Journal of Mental Science* [*J. ment. Sci.*] **96**, 1037–1042, Oct., 1950. 11 refs.

If "methedrine" is as effective in the treatment of depression as electric convulsion therapy (E.C.T.), the advantages to the patient in the saving of risk and discomfort will be obvious. The authors treated 34 consecutive cases, admitted to Carlton Hayes Hospital, Leicester, with a diagnosis of depression, and compared the results with those obtained in a control group of 200 similar cases treated by E.C.T.

The control group was subdivided into six diagnostic categories: (1) involutional depression; (2) neurotic depression; (3) affective psychosis–depressed; (4) atypical affective psychosis with schizophrenic features; (5) involutional depression with paranoid features; (6) affective psychosis—alternating. The last three groups showed a considerably lower discharge rate than the first three. The control group was therefore subdivided into four groups, according to the presence or absence of the following unfavourable prognostic factors: (1) age over 60; (2) duration of illness, before treatment, of over one year; (3) a poor previous personality; (4) a diagnosis of any of the last three in the above diagnostic classification. In no case were all four factors present. The results of treatment were graded as (1) Complete remission. (2) Social recovery: patient discharged with residual symptoms insufficient to prevent him doing some useful work and adjusting himself to domestic life. (3) Improved: symptoms relieved, but not sufficiently to justify discharge. (4) Unchanged, worse, or relapsed within 4 weeks of discharge to a condition as bad as that before treatment.

The 27 women and 7 men treated with methedrine were classified in the same way. The technique of treatment was as described by Rudolf (*J. ment. Sci.*, 1949, **95**, 920). None achieved grade (1), even in the most prognostically favourable group; only 4 achieved grade (2); 7 reached grade (3); and the remaining 23 grade (4). Some of the 34, subsequently treated by E.C.T., reached grades (1) and (2). With methedrine, side-effects such as increased agitation occurred on a dosage insufficient to relieve the depression.

The authors conclude that the therapeutic effectiveness of methedrine compares unfavourably with that of E.C.T. in the treatment of depression. They do point out, however, that methedrine produced relatively better results in the group with the most unfavourable prognosis. They emphasize that, as this group consisted of only 3 patients, the observation must be accepted with reserve, but suggest a use for the drug in the treatment of cases that have not responded to E.C.T. *J. P. Dewsbury*

Infectious Diseases

VIRUS INFECTIONS

1708. **Aureomycin in the Treatment of Influenza. A Controlled Study**
W. G. THALMANN, C. H. KEMPE, J. A. WORRALL, and G. MEIKLEJOHN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 1156–1157, Dec. 2, 1950. 1 ref.

A total of 150 cases of serologically proved influenza-A infection occurred in healthy young men who were engaged in basic military training in the U.S. Army. They were admitted to a military hospital within a period of about 6 weeks, the duration of the epidemic. All appear to have been typical cases of influenza, with 5 showing radiological signs of primary atypical pneumonia. Of the 150 cases 69 were treated with aureomycin (0·25 g. 6-hourly), 43 with penicillin (600,000 units of procaine penicillin intramuscularly once daily), and the remaining 38 were given no chemotherapeutic treatment. The average total dose of aureomycin was 4·2 g., and of penicillin 2,700,000 units.

An analysis of the results is given in tabular form, showing the average duration of illness from the start of symptoms and of stay in hospital, and the average time in hours from the initiation of treatment to a permanent reduction of temperature to 99° F. (37·2° C.) or below, for each of the three groups of patients. The figures for the three groups under each heading are very similar. Thus, the average time elapsing before a permanent fall of temperature was 39·0, 39·5, and 40·6 hours for those given aureomycin, penicillin, and no chemotherapy respectively. These patients were entirely unselected, and showed little evidence of bacterial pathogens in throat and sputum cultures. There was no evidence that either aureomycin or penicillin had any influence on the course of the disease. It is pointed out that a previous report by Finland *et al.* (*Amer. J. Med.*, 1950, **8**, 21), in which aureomycin was claimed to have had good effects in influenza, deals with a series of cases very dissimilar from the present in that they were selected for treatment with the drug on account of the severity of the symptoms and the presence of pulmonary complications. *Reginald St. A. Heathcote*

1709. **Viraemia in Smallpox**
A. W. DOWNIE, K. MCCARTHY, and A. MACDONALD. *Lancet* [*Lancet*] **2**, 513–514, Nov. 11, 1950. 6 refs.

By inoculation on to the chorio-allantois of embryonated eggs, with subsequent passage, it was possible to isolate smallpox virus from the blood of 4 out of 7 patients. The virus was most likely to be present in the blood in the first days of the pre-eruptive fever. Thus in one case 51 infective units per 0·1 ml. of blood were present on the second day, 7 on the third, and none on the fourth day. This patient died on the tenth day.

Virus was not detected in throat swabs taken from a moderately severe case on the first and second days of illness. *R. Hare*

1710. **Laboratory Investigation of Smallpox Patients with Particular Reference to Infectivity in the Early Stages**
F. O. MACCALLUM, C. A. MCPHERSON, and F. D. JOHNSTONE. *Lancet* [*Lancet*] **2**, 514–517, Nov. 11, 1950. 1 fig., 5 refs.

Attempts were made with embryonated eggs to isolate virus from the blood and nose and throat swabs of 13 patients who developed smallpox as a result of contact with a case from the s.s. *Mooltan* in April, 1949. In only 2 out of 8 patients could the virus be isolated from the blood (on the second and third days). The virus was not isolated from the nose swabs from 10 cases, but was recovered from the throat swabs from 2 of the same 10 on the second and third days of the rash. On the other hand the virus was isolated from skin scrapings of the lesions of all 13 patients, and the complement-fixation test, using the scrapings as antigen and immune rabbit serum, was positive in 4 out of 5 patients.

In view of the evident rarity of the virus in the nose and throat of patients who were seriously infected, the authors discuss the possible reasons for this discrepancy in the light of current theories that the disease is transmitted by these secretions. *R. Hare*

1711. **Poliomyelitis. Hospital Enquiry, 1949. Part II**
W. H. BRADLEY and A. H. GALE. *Monthly Bulletin of the Ministry of Health, etc.* [*Mon. Bull. Min. Hlth*] 9, 242–247, Nov., 1950. 2 refs.

In this second part of their report on the Ministry of Health's hospital inquiry into the incidence of poliomyelitis during 1949, the authors summarize the information obtained concerning the effect of pregnancy, tonsillectomy, and cross-infection in hospital on the spread of the disease.

The case fatality among pregnant women suffering from poliomyelitis (69 cases) was 20·3%, while that among women of child-bearing age who were not pregnant (668 cases) was 19·8%. It is thus concluded that pregnancy does not increase the fatality of poliomyelitis.

Only 16 cases were reported in which tonsillectomy had been performed within 2 months of the onset of the disease, this small number being attributed to the reduction in the number of such operations performed during the epidemic. While this group of cases is too small for statistical purposes, it is of interest to note that bulbar paralysis occurred in 8 out of the 16.

Details are given of 12 cases in which it was at least possible that the infection was incurred through contact with another case in a hospital ward. The authors state that such cross-infection appeared to be less frequent in

hospitals for infectious diseases and they suggest that until more is known of the mode of transmission it is not advisable to admit into a general ward any patient who may be incubating poliomyelitis. *Joseph Ellison*

1712. **Investigation on the Care and Treatment of Poliomyelitis Patients. Physiological Studies of Various Treatment Procedures and Mechanical Equipment**
A. G. BOWER, V. R. BENNETT, J. B. DILLON, and B. AXELROD. *Annals of Western Medicine and Surgery* [*Ann. west. Med. Surg.*] **4**, 561–582, Oct., 1950. 45 figs. 686–716, Nov., 1950. 15 figs.

The authors present a comprehensive report dealing with certain new methods which have been developed, mainly at the Los Angeles County Hospital, during the past 3 years for the treatment of cases of poliomyelitis with serious respiratory and circulatory disturbances. The first part of the report embodies a description of the new apparatus which has been devised to maintain adequate ventilation in the patient with acute respiratory involvement. Of these new devices the most important seems to be the Bennett positive-pressure respirator attachment designed to supplement the negative pressure of the Drinker-type tank respirator by the application of positive endotracheal (or mask) pressure during inspiration. This elaborate [and doubtless expensive] apparatus is described with diagrams and illustrations [but there seems little likelihood of its availability in Great Britain in the near future]. Many other refinements [some little more than gadgets] are listed, such as a humidifier attachment to the respirator, a flow-sensitive breathing unit (for intermittent positive-pressure breathing), a respiratory-ventilation meter which measures directly the volumetric flow of any gas, and a physiological cam for the respirator pump which alters the pressure pattern produced by the crank mechanism and produces a more natural type of pressure variation than that usually provided. Other inventions here described include a warning device which sounds an audible signal when an oxygen cylinder is nearly depleted, a special type of collar for use after tracheotomy [this seems worthy of study], improvements in the design of tracheotomy tubes, including an oxygen catheter adapted to the tracheotomy tube, various kinds of suction catheter, and an improved juvenile-size tank respirator.

The second part of the report is devoted to an evaluation of recent developments in treatment. During 1949, 1,128 cases of poliomyelitis were treated at the Los Angeles County Hospital, 130 of these requiring respirator treatment. Tracheotomy was performed in 105 cases, 89 of these being respirator cases. The Bennett positive-pressure attachment was employed in 73 cases. The authors point to a sharp decline in case-fatality during the 1949 epidemic compared with that in the previous 3 years as evidence of the value of the newer methods of treatment: thus the fatality rate for respirator cases in 1946 was 79%, in 1947 67%, in 1948 42%, and in 1949 only 17%.

There follows an elaborate study of the blood chemistry and an analysis of pulmonary ventilation in cases showing various grades of respiratory disability, which provides much information concerning loss and recovery of respiratory function over a period of months. [This portion of the paper is highly technical and will be of interest primarily to physiologists.] The general conclusion is reached that it is of vital importance to take early steps to counteract the progressive decline in respiratory function which occurs in all severe cases.

Finally, the authors consider treatment of the pulmonary atelectasis which may complicate paralysis in poliomyelitis. This condition, it is thought, should be but rarely encountered nowadays if adequate ventilation is maintained throughout the course of the disease. They describe 3 cases from their 130 respirator cases of 1949. These were successfully treated by (1) tracheotomy, (2) bronchoscopy, (3) the use of combined positive and negative pressure, (4) intermittent positive-pressure treatment with penicillin-aerosol (50,000 units in 1 ml. water). Special suction catheters (as described in the first part) were also employed.

[In summarizing this elaborate and highly scientific report it has been possible to draw attention only to some of its main features. Though it is most unlikely that the refinements described will be available for general use in Great Britain in the near future, the report should be studied by all whose field of work lies in this province.] *Joseph Ellison*

See also Sections Hygiene and Public Health, Abstracts 1338; 1345; and Pharmacology and Therapeutics, Abstract 1425.

1713. **Clinical and Virological Studies in Affections of the Nervous System Caused by Mumps Virus.** (Клинико-вирусологические исследования при поражениях нервной системы, вызванных вирусом эпидемического паротита у детей)
S. E. GANZBURG. Клиническая Медицина [*Klin. Med., Mosk.*] **28**, No. 10, 44–50, Oct., 1950. 20 refs.

The author has studied 81 cases of infection of the central nervous system in children due to mumps virus. The diagnosis on admission to hospital ranged from meningitis to food poisoning; in only 13 cases was the diagnosis correct. The age of the patients ranged from 2 to 13 years and most of the cases occurred between February and May. Signs of meningo-encephalitis usually appeared from 3 to 4 days before the onset of parotitis; in 18 cases parotitis was absent. Pathological changes were found in the cerebrospinal fluid in all cases in which examinations were made. The usual finding was an increase in cellular elements; polymorphonuclear leucocytes were found in 74% and neutrophils in 26% of cases; the latter were usually found in the first 4 to 6 days of illness. An increase in protein was found in 34% of cases. The onset of the illness was acute in all cases, with headache and fever; vomiting occurred in 88·5%, and signs of meningeal involvement in 78·6%; epigastric pain, focal symptoms, delirium, convulsions, and coma also occurred. One case was fatal, death occurring in convulsions. Repeated vomiting was a striking feature, and was considered to be a characteristic sign of mumps encephalitis, especially when

accompanied by only a mild degree of meningeal involvement. In laboratory studies, virus was recovered in 2 of 6 cases from cerebrospinal fluid taken on the first and second days of illness; a rise in antibody titre was found in serial serum specimens from 7 cases by means of complement-fixation and haemagglutination-inhibition tests. *D. J. Bauer*

1714. **Studies on the Etiology of Exanthema Subitum (Roseola Infantum)**
C. H. KEMPE, E. B. SHAW, J. R. JACKSON, and H. K. SILVER. *Journal of Pediatrics* [*J. Pediat.*] **37**, 561–568, Oct., 1950. 3 figs., 7 refs.

The authors have studied the transmission of exanthema subitum (roseola infantum) in experiments carried out at the University of California. They describe briefly the clinical characteristics of the disease. The possibility of a virus infection is considered, but attempts to isolate the virus in laboratory animals were unsuccessful. Direct transmission was attempted. Serum from an 18-month-old infant on the third febrile day of what later appeared clinically to be a typical example of the disease was injected intravenously into a 6-month-old recipient. Nine days later typical exanthema subitum developed. The serum was demonstrated to be bacteria-free. Subcutaneous injection of the same serum into 2 rhesus monkeys led in 3 and 4 days respectively to a febrile illness associated in one with a leucopenia. Throat washings taken from the recipient and rendered bacteriologically sterile were sprayed into the nose of 2 other rhesus monkeys, and led to a similar febrile illness and leucopenia, while the serum of these monkeys injected intranasally and subcutaneously into 2 further monkeys caused similar symptoms in one. The same serum passed through a Seitz filter and passed in the same manner into 2 monkeys led in both cases to fever and leucopenia.

Blood clot from the original donor was suspended in saline and passed intranasally and subcutaneously into 2 further monkeys who had recovered from the disease. No further symptoms occurred, but the same material passed into 2 susceptible monkeys led in each case to an identical disease. Serum passaged through fertile hen's eggs was not found to be infective. *H. G. Farquhar*

1715. **The Isolation of Herpes Virus from a Fatal Case of Encephalitis**
L. B. FASTIER and W. S. ALEXANDER. *New Zealand Medical Journal* [*N.Z. med. J.*] **49**, 566–568, Oct., 1950. 1 fig., 2 refs.

BACTERIAL INFECTIONS

1716. **Studies on Tularemia. V. Immunization of Man**
P. J. KADULL, H. R. REAMES, L. L. CORIELL, and L. FOSHAY. *Journal of Immunology* [*J. Immunol.*] **65**, 425–435, Oct., 1950. 1 fig., 16 refs.

A total of 809 persons, including 163 laboratory workers, received one or more prophylactic injections of phenolized or acetone-extracted vaccines of *Pasteurella tularensis*. To avoid severe reactions, persons who had suffered from tularemia, who gave a positive skin test, or whose blood contained circulating agglutinins to *P. tularensis*, were not vaccinated. The others received 4 or 5 subcutaneous injections of doses increasing from 0·05 ml. to 0·5 ml. of vaccine over a period of 7 days. In general, maximum agglutinin titres were reached 3 weeks or so after immunization was begun. As judged by the agglutination titres reached there was no difference between the two vaccines. The patient was examined at 2-monthly intervals by skin testing and determination of the agglutination titre; when the result of his skin test was negative and his agglutination titre had fallen below 1 in 320, he was revaccinated, and thereafter was examined at 6-monthly intervals.

Skin sensitivity induced by vaccination persisted for 2 months in only 20% of patients, and for 6 to 9 months in only 4 persons. Of 72 vaccinated persons who worked with highly virulent *P. tularensis* daily over long periods, 22 developed tularaemia, a far lower percentage than would have been expected from previous experience; it is, however, emphasized that much more strict precautions were taken against infection than had been usual in previous work. The fact that 78% of the cases of tularaemia in vaccinated persons were considerably modified suggests that vaccination conferred partial protection. The authors hold that reactions after vaccination against tularaemia are no more severe than those after typhoid vaccination if precautions are taken to eliminate hypersensitive individuals, and recommend prophylactic vaccination for persons exposed to the organisms. *C. L. Oakley*

1717. **An Outbreak of Plague in an Epidemic Form Treated with Streptomycin and Sulfadiazine.** [In English]
P. K. GHOSH. *Indian Medical Gazette* [*Indian med. Gaz.*] **85**, 441–445, Oct., 1950. 4 refs.

An outbreak of plague in the United Provinces is described. Among 155 patients there were 6 deaths, 4 of which occurred within 16 hours of the start of treatment. Most of the cases were bubonic in type, but in many the lymph nodes involved were in the axillae or cervical region. Patients were given two injections of 0·5 g. of streptomycin, the second injection at an interval of 12 hours, except in 3 cases where the total dose did not exceed 2 g. In addition, sulphadiazine or "sulphatriad" was given in doses of 1 g.

[No exact details of the total sulphonamide dosage are given, but in view of what appears to be the small amount of chemotherapeutic drugs administered the high proportion of recoveries is remarkable.] *G. M. Findlay*

1718. **Modern Therapy of Plague**
K. F. MEYER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 982–985, Nov. 18, 1950. 30 refs.

On the basis of impressive experiences in the laboratory and in field trials, the following modern therapy is recommended in cases in which the presence of plague is suspected.

Streptomycin should be given in large doses (4 g.) at first, but for reasons of economy the dose may be reduced safely on the third and fourth day of recovery. After the fifth day, streptomycin may be replaced by sulfadiazine or sulfamerazine (4 g. daily). In severe septicaemia, and particularly in pneumonic plague, the initial daily dose of 4 g. of streptomycin should be supplemented by oral administration of aureomycin, chloramphenicol or terramycin (2 to 4 g.) and anti-plague immune serum globulin (rabbit) available at the National Institutes of Health. If the patient does not respond to streptomycin and sulfonamide treatment in 2 or 3 days, even when optimal and large initial doses have been given, the infecting strain may be resistant to these antibiotics. In such cases chloramphenicol, aureomycin, terramycin, aerosporin or neomycin may prove beneficial.

When antibiotics are not available, sulfadiazine or sulfamerazine in an initial dose of 4 g., followed by 1 g. every 4 hours for not more than 10 days, has proved highly effective in the treatment of uncomplicated bubonic plague.

Contacts exposed to secondary or primary pneumonic plague should be given 2 or 3 g. of sulfadiazine or sulfamerazine daily for 5 days. With the onset of symptoms, intensive treatment with antibiotics must be instituted.—[Author's summary.]

1719. **Treatment of Whooping-cough with Antibiotics (Streptomycin, Aureomycin, and Chloramphenicol).** (Tratamiento de la tos convulsiva son antibioticos (estreptomicina, aureomicina y cloromicetina))
A. VIDAL FREYRE. *Archivos Argentinos de Pediatria* [*Arch. argent. Pediat.*] **34**, 284–288, Oct., 1950. 6 refs.

Streptomycin was given in the treatment of 20 children with whooping-cough in a dose of 0·5 g. intramuscularly, repeated every 12 hours, to a total of from 3 to 5 g. Results are classified as very good in 4 cases, good in 9, fair in 5, and unsatisfactory in 2. In one of these failures rapid cure was achieved with aureomycin. Chloramphenicol was given to 5 infants and children varying in age from 4 months to 3½ years, and to one adult; aureomycin was given to 9 infants and children aged from 2 months to 7 years of age. The dosage by mouth of chloramphenicol was identical with that of aureomycin: 50 mg. per kg. body weight every 6 hours for the first 2 or 3 days and every 8 hours later. With aureomycin results were excellent in 6, good in 1, and only mediocre in the other 2. With chloramphenicol the results were spectacular and after the third or fourth dose there were practically no further symptoms.

G. M. Findlay

1720. **Lymph-node Culture; a Rapid and Accurate Method for the Bacteriological Diagnosis of Acute Brucellosis.** (L'adéno-culture, méthode rapide et fidèle de diagnostic bactériologique de la brucellose aiguë)
M. JANBON, L. BERTRAND, and H. QUATREFAGES. *Presse Médicale* [*Pr. méd.*] **58**, 1355–1357, Nov. 29, 1950. 1 ref.

In view of the frequent enlargement of the lymph nodes in brucellosis, the authors suggest the removal of a lymph node under strictly aseptic conditions for rapid bacteriological examination as a means of diagnosis. The tissue is ground up and cultivated on "bacto" tryptose agar. After 3 days of incubation the growth of small colonies is visible; these colonies are translucent and have a granular appearance and are identified by direct examination and agglutination. Any culture developing before the third day is due to contamination. Of 53 examinations in 50 cases of brucellosis, 33 (60%) showed a positive result, 12 were negative, and 8 were contaminated. In 18 comparative tests in cases of other diseases the investigations were negative.

Franz Heimann

1721. **Brucellosis of the Urinary Tract**
L. F. GREENE and D. D. ALBERS. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **25**, 638–640, Nov. 8, 1950. 2 refs.

1722. **General Remarks on 300 Cases of Typhoid Fever Treated with Chloramphenicol and Associated Medication** (Remarques générales sur 300 cas de fièvres typhoides traitées par la chloromycétine et les médications associées)
E. BENHAMOU, F. DESTAING, and A. SORREL. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 4107–4108, Oct. 26, 1950.

The results of treating a series of 200 cases of typhoid and paratyphoid fevers in North Africa with chloramphenicol are compared with those obtained in a previous series of 100 cases. The mortality has decreased progressively: of the first 100 patients 86 were cured, of the second 100 patients 94, and of the last 100 cases 98. These increasingly good results are attributed to observance of the following principles. Antibiotic treatment should be begun as soon as the clinical symptoms suggest typhoid fever and before waiting for a bacteriological diagnosis. As a general rule no attempt should be made to give a large loading dose of chloramphenicol: 3 g. in the first 2 hours is quite enough for an adult and is approximately equivalent to 50 mg. per kg. body weight. Aureomycin should be given at the same time as chloramphenicol, as it reduces greatly the risk of collapse. A large loading dose of chloramphenicol may, however, be given without any danger provided the patient's illness has lasted only a few days. After the first week a loading dose should never be given. A dose morning and evening is usually sufficient to produce prompt improvement. For adults 1·5 g. morning and evening, and for children 0·25 g. at the same times, is sufficient dosage. With more effective treatment, relapses have become less common, provided that chloramphenicol has been given in decreasing doses for 14 days after the temperature has reached normal. In the first 100 cases there were 14 relapses: in the second 100 cases 12, and in the third 5. Relapses may occur very late in convalescence, and in 2 cases in the present series developed, with positive blood culture, 60 and 72 days respectively after the temperature had fallen to normal.

It is concluded that ordinary typhoid fever can invariably be cured by chloramphenicol, the temperature returning to normal in 3 days. There are, however, three

complications which do not respond to chloramphenicol alone. These are intestinal complications characterized by meteorism, intestinal haemorrhage, and perforation; cardiac failure, with tachycardia and vascular collapse; and encephalitis with delirium, stupor, and myoclonic contractions. Some evidence is brought forward to show that these symptoms are caused by strains of typhoid bacilli with a low sensitivity to chloramphenicol. The best results are obtained by giving a mixture of chloramphenicol, aureomycin, and sometimes also streptomycin. [It should be noted that chloramphenicol is now known in France as " tyfomycine ".] *G. M. Findlay*

1723. **Preliminary Report on 4 : 4′-Diaminodiphenyl Sulfone (DDS) Treatment of Leprosy**
E. MUIR. *International Journal of Leprosy* [*Int. J. Leprosy*] **18**, 299–308, July–Sept., 1950. 7 refs.

4 : 4′-Diaminodiphenyl sulphone (DDS) is the parent substance of the proprietary sulphones and has hitherto been regarded as too toxic for human use. The drug was given orally in a 2·5% suspension in gum-acacia in ordinary uncomplicated cases of leprosy in doses of 4 mg. per kg. body weight, the average dose being 0·2 g. Intolerance was indicated by anaemia, and necessitated a smaller dose; a small dose was also given to patients who had complications or were very ill, and to those with lepra reactions. In all, 94 cases were treated, divided into three groups: (1) Advanced lepromatous cases with complications such as lepromatous ulcers, blocked nose, eye conditions, and lepra reaction, in which the earlier effects could be suitably tested. (2) Uncomplicated cases in good health. (3) Tuberculoid cases with widespread lesions (5 cases). Clinical and bacteriological improvement was assessed, the latter by study of smears from five suitable skin points by the scraped incision method. Definite clinical improvement was obtained in 24, and considerable improvement in 24, of the 50 cases treated over 9 months; bacteriological improvement occurred in 10 of the same series of cases. Sulphone reactions were seen, similar to lepra reactions except that the former were followed by improvement. Drug fastness was not encountered. It is concluded that DDS is effective, and, with proper precautions, safe; it has the great advantage of cheapness. *J. L. Markson*

1724. **The Intramuscular Administration of Sulphetrone in the Treatment of Leprosy**
—. DHARMENDRA, N. C. DEY, B. ROSE, and P. L. KAPUR. *International Journal of Leprosy* [*Int. J. Leprosy*] **18**, 309–331, July–Sept., 1950. 4 figs., 7 refs.

The defective absorption of the sulphone drugs from the alimentary tract, and their high cost, prompted a detailed investigation into the parenteral administration of sulphetrone. Six preparations of the powder were used: an aqueous solution, suspensions in hydnocarpus and arachis oils with and without wax, an emulsion of hydnocarpus oil, and the watery solution. It was found that 0·05 g. of the drug in aqueous solution was the smallest amount consistently producing a detectable blood concentration, which was 0·5 mg. per 100 ml. in 2 hours. With doses of 0·6 g. and 2 g. in the watery solution and the oily suspension measurable amounts of the drug appeared in the blood in 5 minutes, while the highest concentration occurred at 2 hours. After doses of 0·1 to 0·3 g. the blood was clear of the drug in 24 hours, after 0·6 to 1·5 g. in 48 hours, and after 2 g. in 72 hours. Absorption of oily suspensions was rather slower than that of the watery solution, which gave higher initial levels which, however, were maintained for the same period. A comparison of the blood levels after oral and intramuscular administration showed that one-fifth of the oral dose, given intramuscularly, gave comparable concentrations. With regard to the urinary excretion, the drug appeared in the urine in one hour with all doses and preparations, the peak period being at 2 to 3 hours. With a dose of 0·3 g. a concentration of 3 to 5 mg. per 100 ml. was found after 24 hours, after 48 hours with doses up to 1 g., and after 72 hours with doses up to 2 g.; 70 to 80% of the drug was excreted in 5 days with the watery solutions, and slightly less with the others. Half was excreted in the first 24 hours. The urinary concentration of the drug was about 10 times as high as that in the blood, while the concentration in the skin approximated to that in the blood. The aqueous solution of sulphetrone was considered to be the best preparation, followed by the emulsion in hydnocarpus oil. The most suitable dosage is probably 1 g. daily, but higher doses may be given less frequently. On this regime, marked clinical and bacteriological improvement has been noted. Toxic effects included fever, nausea, weakness, giddiness, and cyanosis, all of which soon disappeared. Anaemia was slight and did not necessitate withdrawal of the drug. It is considered that the intramuscular administration of sulphetrone is safe and effective, requiring a weekly dose of only 4 to 5 g., compared with the 30 g. required for the oral route.
J. L. Markson

1725. **Studies of the Absorption, Excretion, and Distribution in the Body of the Sulfones used in the Treatment of Leprosy**
H. ROSS. *International Journal of Leprosy* [*Int. J. Leprosy*] **18**, 333–344, July–Sept., 1950. 8 refs.

The absorption, excretion, and distribution of the sulphones promin, diasone, promacetin, and sulphetrone were studied in 32 patients who had been taking these drugs for a period of from 4 months to 7 years. Blood, urinary, faecal, and skin concentrations were determined, skin biopsy specimens being obtained under analgesia with " metycaine " which, unlike procaine, does not give a colour reaction in the Bratton–Marshall test. Tissue was also obtained from orthopaedic cases at operation, and the sulphone content of the viscera was determined in 6 patients post mortem.

Detailed results are given. These drugs are retained in the body up to 14 days after the cessation of treatment, and occasionally up to 4 weeks, while the distribution of promin, given intravenously, was similar to that of the other drugs, which were given orally. Diasone, promacetin, and sulphetrone appeared in appreciable amounts in the faeces, suggesting incomplete absorption—a conclusion which is borne out by the absence from the faeces of promin, given intravenously. These drugs are

excreted mostly by the kidneys, but apart from the variation caused by differences in absorption and in renal function there was a marked individual variation, even with similar doses. Skin concentrations differed little from the blood concentrations, and no difference was found between the concentrations in normal and lepromatous skin. Evidence of storage was found in muscle, liver, spleen, kidneys, skin, and nerves.

J. L. Markson

See also Section Microbiology, Abstract 1499.

TUBERCULOSIS

1726. **A Comparison between Precultural Acid and Alkali Treatment of Tuberculous Material.** (Dyrking av tuberkuløst materiale. Natronlut-eller svovelsyre-behandling?)
S. T. MADSEN. *Nordisk Medicin* [*Nord. Med.*] **44**, 1870–1871, Nov. 24, 1950. 4 refs.

At the Gades Institute, Bergen, a comparison was made, with 5,479 specimens of tuberculous material, between the acid and alkaline methods of concentration before culture. Material treated with 4% sodium hydroxide was found to yield 2% more positive cultures than the same material treated with 6% sulphuric acid despite a slightly higher rate of contamination with non-acid-fast organisms. *J. E. M. Whitehead*

1727. **Primary Complex of Pulmonary Tuberculosis**
A. D. BIGGS. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **80**, 566–577, Oct., 1950. 10 figs., 3 refs.

This study of the natural history of primary tuberculosis is based on the findings in 142 children with primary tuberculosis attending the out-patient department of St. Luke's Hospital, Chicago. The diagnosis was made as a result of investigations carried out on all children who were found on routine tuberculin testing to give a positive reaction and have been followed up for 5 years or more. More than half were under observation at frequent intervals throughout the period. A detailed history was taken and a full examination performed each month at first, and less frequently when the disease was thought to be quiescent. None of the minor disturbances of health (such as low-grade fever, cough, and failure to gain weight) which are usually thought to occur in patients with primary tuberculosis were encountered, except in 3 patients with massive radiological shadows in the lung fields. The investigations undertaken included height and weight records, blood count, erythrocyte sedimentation rate, and examination of gastric washings, all of which in over 90% of the patients gave normal results. The accepted radiological features of primary tuberculosis—transient shadows in the lung fields and enlargement of hilar lymph nodes—were present in all cases. Of 88 patients followed up for 5 years without interruption, calcification occurred in the peripheral lung fields in 25%, and in the hilar nodes in 93%. This calcification was usually first observed about 12 months after the initial *x* ray had been taken, and during the following 3 years it became more pronounced.

The only treatment necessary in the majority of cases was to remove the child from the source of contact, if known (such a source was detected in only one-third of the cases) and to ensure that an adequate diet was taken. The patients were not isolated, the possibility of spread of infection to tuberculin-negative children being considered remote. *R. M. Todd*

1728. **Selective Bronchography with a Métras Catheter and Water-soluble Contrast Medium in Pulmonary Tuberculosis.** (Die gezielte Bronchographie mit Métras-Kathetern und einem wasserlöslichen Kontrastmittel bei Lungentuberkulose)
R. HOPPE and W. MAASSEN. *Tuberkulosearzt* [*Tuberkulosearzt*] **4**, 708–718, Dec., 1950. 5 figs., 20 refs.

The new bronchographic method here described makes use of a water-soluble, viscous contrast medium, " per-abrodil M ", in 50% concentration. In contrast to iodized oil this substance is quickly eliminated, being easily absorbed by the lung parenchyma. Hereby the risk of the contrast medium causing intracanalicular spread is reduced to a minimum. The water-soluble fluid mixes readily with the bronchial secretion and penetrates easily into the bronchioles and through passages narrowed by stenosis. The contrast medium is injected directly into the selected area through a Métras catheter. This semi-rigid tube, which is either straight or curved at the end, has a radio-opaque tip which permits of its insertion under *x*-ray control. Thorough anaesthesia with 2 to 4 ml. of 2% butethanol through a curved laryngeal cannula is essential. With this method even the bronchus to the upper lobe can be filled in the upright position.

Normal filling of bronchi and alveoli excludes tuberculosis within the area visualized. Bronchography, though unsuitable for the demonstration of cavities, shows up bronchiectasis and bronchial stenosis where ordinary radiography and tomography have failed. Another important field for bronchography is in cases of bronchial stenosis situated beyond the range of bronchoscopy. Of a series of 25 cases of all forms of pulmonary tuberculosis, with collapse in approximately 50%, bronchography demonstrated the presence of bronchial stenosis, bronchiectasis, or both in three-quarters, appearances being normal in the remainder.

Bronchography is contraindicated in the following tuberculous conditions: febrile and mainly exudative cases, early infiltration, early cavitation, freshly spreading cavernous processes with more than 4 oz. (120 ml.) of sputum a day, haemoptysis, laryngeal tuberculosis, recent induction of pneumothorax, and recent pneumolysis. A poor general condition and a tendency to allergic reactions, thyrotoxicosis, and acute and decompensated heart or renal failure are also contraindications. Bronchograms of the upper lobe, reproduced, demonstrate the position of the catheter and illustrate the potentialities of the new method. *E. G. W. Hoffstaedt*

1729. **The Efficiency of Different Laboratory Examination in the Diagnosis of Pulmonary Tuberculosis**
D. HATA, H. D. VENTNERS, and M. M. CUMMINGS. *Diseases of the Chest* [*Dis. Chest*] **18**, 352–362, Oct., 1950. 12 refs.

An interesting account is given of the investigation of 107 patients with signs or symptoms of pulmonary tuberculosis, in which attempts were made to culture tubercle bacilli from sputum, gastric washings, laryngeal swabs, and urine. Positive cultures were obtained from 43·9% of undiluted gastric-washing specimens, compared with 37·7% of specimens of sputum and 16·9% of laryngeal swabs examined. It is concluded that gastric-content examination is the most sensitive method available for detecting tubercle bacilli in cases of suspected pulmonary tuberculosis. *Kenneth Marsh*

1730. **Hypokalaemia Complicating Sodium *para*-Aminosalicylate Therapy for Pulmonary Tuberculosis**
K. H. HEARD, A. H. CAMPBELL, and J. J. HURLEY. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 606–612, Oct. 21, 1950. 4 figs., 5 refs.

Of 60 patients with pulmonary tuberculosis treated with sodium *para*- aminosalicylate at the Repatriation General Hospital, Heidelberg, Victoria, 12 were thought to have developed hypokalaemia and these cases are described in detail in this preliminary report. In 6 cases there was clinical, biochemical, and electrocardiographic evidence of hypokalaemia, but in the others the evidence was incomplete. There were 4 cases of sudden death, the first patient being a man of 74 with multiple extra-systoles and a low serum potassium level, and the second a man of 42 with muscular weakness and incontinence, on whom no relevant investigations were carried out before death, and in whom post-mortem examination revealed no cause for death. The third of these patients, a man of 49, had electrocardiographic signs of potassium deficiency, but necropsy revealed a small septal myocardial infarct; while the fourth, a man of 26 with progressive and extensive pulmonary disease, had no clinical or biochemical evidence of hypokalaemia. The last 2 cases were included in the series because it was considered that the mode of death was that which occurs in hypokalaemia.

The main symptoms of hypokalaemia in these cases were muscular weakness and pains (which occurred in 5 cases), drowsiness, and mental dullness. No definite threshold level of serum potassium was associated with the development of the pareses. Electrocardiographic changes were found in 7 cases, the chief abnormality being depression of the S–T segment with broadening of the T wave. Multiple extra-systoles, auricular and/or ventricular, were present in 4 cases, the latter being of serious import. There was a striking correlation between the electrocardiographic and biochemical findings. The treatment was to suspend administration of the drug and to give varying amounts of potassium chloride (24 to 30 g. daily), all cases other than the fatal ones recovering completely in from 2 to 14 days.

The cause of the hypokalaemia was not clear, though it was considered most likely that either the *para*-aminosalicylate itself or some impurity in the drug was responsible. However, it was noted that several of the patients had a poor appetite and hence possibly a low potassium intake. The authors suggest that the use of potassium *para*-aminosalicylate, or the concurrent administration of potassium chloride and sodium *para*-aminosalicylate may prevent this condition developing. *A. G. Beckett*

1731. **Preliminary Report of Clinical Experience with *p*-Aminosalicylic Acid**
N. H. DEJANNEY, J. COX, and E. GRINDELL-BALCHUM. *Diseases of the Chest* [*Dis. Chest*] **18**, 413–429, Nov., 1950. 3 figs., 26 refs.

The authors studied the therapeutic response in 42 cases of tuberculosis to orally-administered *p*-aminosalicylic acid (PAS), 40 of the patients having advanced pulmonary disease, mostly bilateral and cavernous, and 2 tuberculous meningitis; all had failed to respond to prolonged courses of streptomycin.

In the early stages of the study a dose of 15 g. daily was given, but this amount was not well tolerated and was later reduced to 10 g. daily for periods ranging from 30 to 150 days. The uncoated tablet of the free acid was the preparation used, and even with the lower dosage toxic manifestations, in the form of gastro-intestinal upset and loss of weight, were not infrequent.

The toxic effects of the drug were more than offset, however, by the definite symptomatic relief experienced by most patients. Of the 40 patients with pulmonary disease 20 showed improvement as judged by fall in temperature, reduction in cough and sputum, and a feeling of well-being (in a few cases the improvement was not maintained beyond 4 months from the commencement of treatment, and this adverse change was ascribed to the development of resistance by the infecting tubercle bacilli); 5 patients were relatively symptom-free before treatment and an assessment on clinical grounds could not be made; and the remaining 15 patients showed no clinical improvement, but all had extensive disease with a hopeless prognosis.

Radiological improvement was noted in 21 cases treated with PAS alone and in 6 cases in which other forms of treatment were also given; the remaining 13 showed no change or progression of the disease. Endobronchial lesions complicating pulmonary disease responded extremely well to PAS therapy.

The 2 patients with meningeal tuberculosis had relapsed following streptomycin treatment. Both patients derived marked benefit from PAS administered concurrently with a further course of streptomycin. *G. B. Forbes*

1732. **Treatment of Pulmonary Tuberculosis with Streptomycin and *para*-Aminosalicylic Acid**
MEDICAL RESEARCH COUNCIL. *British Medical Journal* [*Brit. med. J.*] **2**, 1073–1085, Nov. 11, 1950. 6 figs., 8 refs.

This is the long-awaited report of the Medical Research Council on the treatment of pulmonary tuberculosis with streptomycin and *para*-aminosalicylic acid (PAS).

Chest physicians throughout Britain were invited to submit cases of pulmonary tuberculosis to the Trials

Committee; if considered suitable the cases were admitted, usually within 2 weeks, to one of 10 hospitals acting as centres for this trial. Cases selected were of acute, progressive, bilateral tuberculosis of recent origin, bacteriologically proved, unsuitable for collapse therapy, and in subjects between the ages of 15 and 30 years. Patients were assigned to one of three groups by random sampling. Before treatment each was observed for one week in hospital.

Out of 166 patients 59 received PAS (P group), 53 both streptomycin and PAS (SP group) and 54 streptomycin alone (S group). Streptomycin was given as one daily injection of 1 g., and PAS was given as the sodium salt in 20-g. doses daily. All patients received chemotherapy for 3 months, but observation was continued for a further 3 months after conclusion of the course. No treatment other than rest in bed was instituted until one month after completion of the course of chemotherapy.

A fourth group was used for comparison of results. This group was taken from the first M.R.C. trial of streptomycin (*Brit. med. J.*, 1948, **2**, 769) and was treated solely by rest in bed.

In each group during the period of treatment one death occurred; these figures were not considered statistically significant, but the fatality rate of 3% in the P group compares favourably with a 27% fatality rate in the control group. Radiological improvement occurred in 56% of the P group, 74% of the S group and 87% of the SP group. From the clinical aspect it was found that the higher the fever and the greater the extent of cavitation, the worse the prognosis. The bacterial content of the sputum was most reduced in the SP group. On the whole PAS appeared to be less effective than streptomycin; the improvement seen in the SP group was slightly greater than in the S group. The most valuable effect of combination of streptomycin and PAS was the low incidence of drug resistance. Strains with a streptomycin-resistance ratio above 8 were found in 33 of 49 cases in the S group, and in only 5 of 48 in the SP group.

R. H. J. Fanthorpe

1733. **Treatment with Streptomycin and *p*-Aminosalicylic Acid of Active Open Tuberculosis associated with Silicosis.** (La terapia con streptomicin e acido *para*aminosalicilico della tubercolosi attiva ed aperta associata alla silicosa polmonare)

A. Boselli and C. Lusardi. *Medicina del Lavoro* [*Med. d. Lavoro*] **41**, 268–277, Oct., 1950. 17 refs.

A description is given of 23 cases of tuberculosis of the lung associated with silicosis which were treated with streptomycin and *para*-aminosalicylic acid (PAS), either together or separately. In 14 cases the tuberculosis had developed after the silicosis was established, whereas in the other 9 cases the lesions were of a mixed nature probably from the early stages of the disease. The sputum was positive in all cases. Although streptomycin gave good results at first, it was noted that in some patients a resistance to the drug developed after some weeks and fever, which had ceased, recurred. The addition of PAS gave good results, though one patient could not take it owing to gastric intolerance. It seemed eventually that the best results were obtainable if PAS were given first and streptomycin added after an interval. The total dose of the former varied from 200 to 1,800 g., and of the latter from 15 to 70 g.

In 12 out of 14 cases in which the tuberculosis had developed in an initially silicotic lung the results of treatment were good, though since in some cases surgical treatment was also given, evaluation of the results is not easy. Where tuberculous and silicotic lesions were intimately mixed the results in 4 out of 6 patients were negligible and in the other 2 the response was slight. But in none of the 23 cases was treatment entirely without benefit. When cavities were present healing by scarring was rarely seen. When cavitation was absent the improvement was more marked. Though some months have elapsed since these patients were treated, they all continue to experience some relief. *G. C. Pether*

1734. **BCG Vaccination in Silicosis**

A. J. Vorwald, M. Dworski, P. C. Pratt, and A. B. Delahant. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 455–474, Nov., 1950. 20 figs., 20 refs.

It is known that the inhalation of crystalline free silica decreases resistance to pulmonary tuberculosis. Since there is evidence that B.C.G. vaccination may reduce tuberculous morbidity in persons with low natural resistance to the disease and may therefore provide a means of reducing the incidence of tuberculosis in association with silicosis, the authors have studied the course of infections with B.C.G. in animals exposed to silica dust, and the degree of protection afforded by vaccination with B.C.G. in developing tuberculosilicosis in an impressive series of carefully designed experiments.

In the first experiment 25 guinea-pigs were infected by intracutaneous injection with B.C.G. and simultaneously exposed to a high atmospheric concentration of quartz dust, and a control group was infected in like manner and kept in normal air; spreading tuberculous lesions occurred in 11 of the former group and in only one of the 18 controls. The second experiment was similar to the first except that the B.C.G. infection was given by inhalation; 12 of the 25 animals exposed to quartz dust developed progressive and fatal tuberculosilicosis, while the unexposed controls remained free of pulmonary tuberculosis. Similarly, when an infection with B.C.G. was induced by inhalation in 25 animals which had previously been exposed for 4 months to quartz dust, 19 developed progressive tuberculosilicosis, whereas none of the unexposed controls were affected. In a fourth experiment 25 guinea-pigs were vaccinated intracutaneously with B.C.G.; 2 months later they were infected by inhalation with human tubercle bacilli (attenuated strain R_1) and then exposed to quartz dust. None of these animals escaped tuberculous disease, whereas in a control group similarly infected but not exposed to quartz dust only 2 of 25 developed tuberculous lesions.

B.C.G. organisms recovered from the tissues of animals developing progressive disease in these experiments had not been altered by growth in silicotic tissue, for they showed no enhancement of virulence when subinoculated in large doses into healthy guinea-pigs. The authors

conclude that the resistance of the host can be lowered by the tissue reaction to quartz particles to such an extent that the B.C.G. organisms in the dose used for vaccination are able to produce progressive and fatal pulmonary disease. An additional important finding was the isolation of viable B.C.G. organisms from the lungs and lymph nodes of the animals up to 18 months after their injection. On the sum of the evidence, B.C.G. vaccination would appear to be contraindicated in persons who might at some time be exposed to quartz dust; but the authors urge caution in interpreting these experimental results in terms of human experience.

[This is an extremely important paper, which should be read in the original.] *M. Daniels*

1735. Immunization Studies with Irradiated Tuberculosis Vaccines

R. W. SARBER, W. J. NUNGESTER, and F. D. STIMPERT. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **62**, 418–427, Oct., 1950. 9 refs.

The chief disadvantage of B.C.G. vaccine is the short life of the culture; it is thus difficult to prepare, to test for safety and sterility, and to distribute and administer within a week. The experiments recorded in this paper compare the durability and immunizing effects of a vaccine of a virulent human tubercle bacillus that had been irradiated with ultraviolet light with those of B.C.G.

A virulent strain of human tubercle bacillus was grown in a liquid synthetic medium for 12 days. The culture was then partially dried aseptically on filter paper, resuspended in saline, homogenized by shaking with glass beads, filtered, and finally diluted to contain 1 mg. of semi-moist weight of organisms per ml. Immediately after preparation the suspensions were irradiated with ultraviolet light, previous experiments having been made to determine the minimum period of irradiation that would consistently kill all the organisms. Samples were taken for safety and sterility tests, and thiomersolate was added as a preservative. A strain of B.C.G. was similarly treated, except that a non-irradiated vaccine was prepared as well.

Guinea-pigs were tested with 0·005 mg. of P.P.D. and all negative reactors were divided into two groups. In one group each animal received 5 ml. of irradiated vaccine (5 mg. of organisms) at weekly intervals for 3 weeks. The other group received the same dosage of non-irradiated B.C.G. An equal number of animals served as controls. Three weeks after the last immunizing dose each animal received intraperitoneally 1 mg. of the same virulent human tubercle bacilli prepared as for the vaccine but not irradiated. The animals were kept for 4 months, after which time they were killed and examined. The results are given in tables and are shown as percentage of survivors and as evaluated by the Feldman index. In the group treated with the irradiated virulent human tubercle bacillus 68% of the guinea-pigs survived, with B.C.G. 60%, with irradiated B.C.G. 12%, and of the controls 29%.

Further experiments of a similar character were made with other virulent human tubercle bacilli as the test organism after immunization. The results are given in the same way. It is known that the irradiated vaccine will keep for at least one month, for none was used until one month after it was made. *A. G. S. Heathcote*

1736. Tuberculosis in Student Nurses and Medical Students at the University of Wisconsin

H. A. DICKIE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 941–959, Oct., 1950. 1 fig., 11 refs.

Since 1933 the Student Health Service of the University of Wisconsin has been investigating the incidence of tuberculosis among medical students and student nurses. Nearly all students were tested on entering the schools, first with 1 unit of tuberculin and then, if negative, with 100 units. Students who gave negative reactions were retested at 6-monthly intervals. Radiographs were taken on admission and on graduation, and also every 6 months in the case of reactors. After October, 1942, B.C.G. vaccination was made available to those whose reaction was negative. The multiple-puncture technique was used on 245 medical students and 174 student nurses; all but 2 gave a positive reaction. There were no systemic reactions, local abscesses, or regional adenitis. Tuberculin sensitivity on entry varied for nurses from 8% to 42%, and for students from 22% to 43%. The percentage of students who gave negative reactions on entry and positive during training varied from 14 to 42; there was no decline in the conversion rate in the period before the use of B.C.G.

The author has studied the tuberculous morbidity in these different groups. He rightly stresses that morbidity among those tuberculin-negative should be considered especially in respect of those who converted to positive. [There is some confusion in the statistics, for the proportion of conversions given in the analysis at this point is greater than that given earlier.] Of 33 nurses who gave positive reactions on entry, 1 developed tuberculosis; of 89 nurses who were negative on entry, 59 converted to positive, and of these 8 developed tuberculosis.

Among medical students entering from 1934 to 1943, 95 were positive on entry, and tuberculous lesions developed in 2 of these; 188 were negative on entry, 138 converted to positive, and of these 19 developed tuberculosis. Among medical students entering from 1944 to 1947, 46 were positive on entry and 2 developed tuberculosis; 106 were negative and received B.C.G. vaccine and of these 1 developed a tuberculous lesion; 44 were negative and were not vaccinated, 34 converting to positive, among whom tuberculosis developed in 6. The results add strong support to the thesis that B.C.G. vaccination undoubtedly reduces the morbidity closely following primary tuberculous infection.

M. Daniels

1737. Riboflavin, Nitrogen, and Thiamine Metabolism of Women with Active Tuberculosis

W. D. BREWER, H. L. TOBEY, DA HWEI PENG KAN, M. A. OHLSON, and C. J. STRINGER. *Journal of the American Dietetic Association* [*J. Amer. diet. Ass.*] **26**, 861–867, Nov., 1950. 2 figs., 31 refs.

1738. **Effects of Antimicrobial Agents on the Tubercle Bacillus and on Experimental Tuberculosis**
W. STEENKEN and E. WOLINSKY. *American Journal of Medicine* [*Amer. J. Med.*] **9**, 633–653, Nov., 1950. 2 figs., bibliography.

PROTOZOAL INFECTIONS

1739. **Aureomycin in the Treatment of Acute Evolutive Intestinal Amoebiasis.** (L'auréomycine dans le traitement de l'amibiase intestinale aiguë, évolutive)
F. SIGUIER, —. CHOUBRAC, M. PIETTE, and J. HERMAN. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **66**, 1363–1369, Oct. 20, 1950. 2 refs.

The authors record the treatment of 40 cases of amoebic dysentery with aureomycin. The infection was contracted overseas in all but one case; 35 were cases of relapse (33 of these had been repatriated from the Far East) and 5 were primary cases. Treatment consisted of 20 to 30 g. of aureomycin given orally during 7 to 10 days; 1·5 to 2 g. was given on the first day and 3 g. on following days. The drug was well tolerated, only 4 patients having minor disturbances. The action of the drug was rapid; after 3 to 4 days of treatment the dysentery had disappeared, and in less than a week the ulceration of the mucosa had healed. In 35 of these cases a clinical cure was obtained, the ulcers being healed and the stools free from amoebae. In 2 cases amoebae and cysts reappeared in the stools and one patient still suffered from disturbances attributed to the disease, although the stools were negative. Two others were lost to sight after treatment. *R. A. Neal*

1740. **Relapse of Kala-azar after Splenectomy**
A. DAS and P. C. SEN GUPTA. *Lancet* [*Lancet*] **2**, 681–682, Dec. 2, 1950. 18 refs.

From Calcutta a description is given of a case of antimony-resistant kala-azar in which splenectomy failed to eradicate the infection. The patient had his first attack of fever in 1940; kala-azar was diagnosed in 1941 and treated with urea stibamine. He relapsed after 3 months and was treated with sodium antimony gluconate with symptomatic improvement. In 1943 he relapsed again, with jaundice and splenomegaly. In spite of antimonials his spleen remained enlarged. In 1947 he had further antimony treatment without effect on the size of the spleen. Splenectomy was performed, after which he was in good health for 4 months. There was a further relapse in 1948, during which Leishman–Donovan bodies were found in the bone-marrow smears. A course of urea stibamine was followed by some improvement, although the infection still persisted in the bone marrow. A course of pentamidine did not arrest his downward progress, polyserositis developed, and the patient died in March, 1949.

The authors review the literature of splenectomy in the treatment of kala-azar. The operation is only performed nowadays in drug-resistant cases. In 6 such cases reported in the literature there were 4 cures and 2 failures. In view of the probability that successes tend to be reported and failures suppressed, the authors attach no statistical significance to these figures. Theoretically, the enlarged spleen forms a reservoir of infection probably beyond the reach of drugs, and this is no doubt the major cause of the concomitant anaemia in the disease. Nevertheless, the operation should only be considered in cases in which intensive and protracted therapy with antimonials and the aromatic diamidines has failed. Even after splenectomy in drug-resistant cases, the above therapy should be continued. *William Hughes*

1741. **Cutaneous Leishmaniasis. Report of Cases Occurring in Great Britain and the United States**
A. H. CONRAD, R. C. MANSON, and G. A. G. PETERKIN. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 502–509, Oct., 1950. 4 figs.

1742. **Proof of the Existence of *Trypanosoma rangeli* in Chile.** (Comprobacion de la existencia de *Trypanosoma rangeli* en Chile)
R. GAJARDO and S. E. THIERMANN. *Revista Médica de Valparaiso* [*Rev. méd. Valparaiso*] **3**, 234–236, Nov., 1950. 1 fig., 5 refs.

Trypanosoma rangeli, which has already been seen in Venezuela and Guatemala, has been found in Chile infesting *triatoma* which also transmits *T. cruzi*, the causal agent of Chagas's disease. It is believed that *T. rangeli* has been seen in the blood of a patient in Chile.
G. M. Findlay

1743. **Effect of Phenylhydrazine Hydrochloride on *Plasmodium knowlesi* Infection in the Monkey**
R. H. RIGDON, D. W. MICKS, and D. BRESLIN. *American Journal of Hygiene* [*Amer. J. Hyg.*] **52**, 308–322, Nov., 1950. 7 figs., 12 refs.

Experiments on 25 *Macaca mulatta* monkeys showed that the oral administration of phenylhydrazine controls the acute phase of a blood-induced *Plasmodium knowlesi* infection. After the intravenous or subcutaneous inoculation of infected blood, the monkeys, 2·3 to 4·5 kg. in weight, were dosed orally with a solution of phenylhydrazine hydrochloride in 95% ethyl alcohol at a concentration of 1 g. per 50 ml. Severe anaemia was produced in normal monkeys by a dose of 150 mg., while an extended course of treatment with doses in the region of 100 mg. produced no great toxic reaction, the erythrocyte count returning to normal at the end of treatment. The largest amount given was 1·19 g. in 13 doses over a period of 27 days.

Twelve infected monkeys were treated with various courses of the drug and the degree of parasitaemia and the erythrocyte count were recorded throughout the experiments. Three died of parasitaemia during treatment and a fourth was found moribund and was killed. As a result of these experiments it appears that all monkeys treated with 100 to 150 mg. of phenylhydrazine when the parasites first appear in the blood, followed by 2 doses of 50 mg. at 3- to 5-day intervals, recover from the acute infection. Parasites could still be demonstrated in the blood 2 to 3 months later, but the number

was usually less than 1 per 500 erythrocytes. The maximum effect of phenylhydrazine appears in approximately 18 hours and persists for 48 to 72 hours. Two infected monkeys were treated with the drug and, after recovering from the acute infection, were subjected to splenectomy. Neither animal developed a recurrence, but when a second inoculation was given they promptly developed an infection. This suggests that the phenylhydrazine effected a cure of the first infection. Four splenectomized monkeys were infected and the resulting infections were treated with normally adequate doses of the drug. All died of infection within 14 to 27 days, indicating that the response to phenylhydrazine is dependent on the presence of the spleen.

The authors describe degenerative changes which appear in the parasites after phenylhydrazine treatment and discuss the mechanism of action of the drug. It is suggested that the irreversible changes produced by phenylhydrazine in the erythrocyte are primarily responsible for its effect on the parasite. *I. M. Rollo*

1744. **Study in the Entomology and Oecology of Foci of Malaria in Styria.** (Entomologischökologische Untersuchungen an steirischen Malariaherden)
E. KUPKA and M. ANSCHAU. *Acta Tropica* [*Acta trop., Basel*] **7**, 298–314, 1950. 2 figs., 25 refs.

1745. **Coronary Occlusion Syndrome in Acute Falciparum Malaria.** [In English]
K. S. MATHUR. *Indian Heart Journal* [*Indian Heart J.*] **2**, 130–137, May, 1950. 3 figs., 24 refs.

OTHER INFECTIONS

1746. **An Outbreak of Primary Pulmonary Coccidioidomycosis in Los Angeles County, California**
M. D. KRITZER, M. BIDDLE, and J. F. KESSEL. *Annals of Internal Medicine* [*Ann. intern. Med.*] **33**, 960–990, Oct., 1950. 5 figs., bibliography.

Until recently the San Joaquin valley was the only area of the United States in which coccidioidomycosis was known to be endemic, but other areas of the southwestern States are now known to harbour the disease. The authors have obtained evidence of the existence of a new area of endemicity as a result of an outbreak of primary pulmonary coccidioidomycosis amongst a group of 61 young men in a forestry camp within the area of Los Angeles county, which had hitherto been regarded as free. This outbreak provided special opportunities for epidemiological study, occurring in a community of young men of uniform age whose period of residence in the area was definite, whose work was similar, and whose activities were well documented. The disease was first diagnosed in 3 patients admitted to the Los Angeles County Hospital from the camp, and as other cases of a similar nature had occurred at the same time an investigation of the entire group was undertaken. Serial skin tests and precipitin and complement-fixation tests were carried out, as a result of which 4 additional active cases were detected. While this investigation was in progress a further 45 men were transferred from another camp outside the area, providing a useful control group. After eliminating from each group those who had previously lived in an endemic area the incidence of positive skin reactions among the original group was found to be significantly higher than among the controls, the figures being 16 out of 57 (29%) and 3 out of 43 (7%) respectively. Moreover, of the 20 positive reactions obtained among the whole original group of 61, 7 (35%) developed during the period of the investigation in subjects who had previously given a negative reaction. It was therefore concluded that adequate evidence existed of the endemicity of the disease in that area.

The authors are satisfied that the positive complement-fixation test provides very reliable evidence of either past or recurrent active infection; they discuss suitable dilutions of antigen for skin test purposes: in the presence of a particular " geographical " history accompanied by an upper respiratory infection, the most useful diagnostic procedure is a skin test in the 1 in 100 dilution; if this is negative the 1 in 10 dilution should be used, except in patients with allergic manifestations (erythema nodosum) when a 1 in 1,000 dilution is safer.

In following the course of the 7 patients admitted to hospital reliance was placed on serial radiography and serial complement-fixation tests. The authors found it unnecessary to keep the patients at absolute rest in bed for months at a time. They permitted gradual ambulation in patients who were symptom-free, and conclude that treatment with rest in bed at home can be carried out successfully.

[This paper is of special value because it provides an excellent review of the literature.] *W. H. Bradley*

1747. **Disseminated Mycotic Disease. Report of Three Cases**
O. J. PARRILLO. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 747–749, Oct. 28, 1950. 5 figs., 1 ref.

The author first describes a case of disseminated torulosis of which the first sign was cervical adenopathy. A diagnosis of reticulum-cell sarcoma was made and radiotherapy given. Three years later the patient developed pleurisy with effusion, generalized lymphadenitis, and splenomegaly. A diagnosis of Hodgkin's disease was now made from axillary lymph-node biopsy. Improvement again resulted from radiotherapy. Later, signs suggesting cerebral involvement were noted, and death occurred during a further course of radiotherapy. At necropsy a large number of granulomatous lesions were found in many organs and histological examination revealed systemic torulosis.

A second patient had had diarrhoea since childhood. At the age of 31 he had pneumonia which left him with a productive cough. Five years later he was admitted to hospital and radiography revealed infiltration in the upper lobe of the right lung and constrictions and ulceration in the large bowel. On proctoscopic examination a granulomatous mass was found in the rectum, and histological examination of this showed large multinucleated phagocytic cells containing *Histoplasma*

capsulatum. At necropsy widespread involvement of the internal organs and lymph nodes was found. There was an abscess cavity in the upper lobe of the right lung. Many small discrete abscesses were present throughout the lungs and other organs.

A third patient was admitted to hospital for right-sided upper abdominal pain, sweats, and pyrexia. Serial radiographs indicated increasing infiltration of both lungs. Later he developed cerebral symptoms. Culture of the spinal fluid and blood on Sabouraud's medium yielded yeast-like organisms morphologically resembling *Candida albicans*. At necropsy all internal organs and the central nervous system were seen to be involved.

It is stressed that disseminated mycotic disease may mimic other obscure diseases, and the causative organisms should be sought in biopsy specimens or in body fluids.

Geoffrey McComas

1748. **Mycotic Meningo-encephalitis.** (Mycoses cérébro-méningées)

C. ATTAL. *Annales de Médecine* [*Ann. Méd.*] **51**, 445–494, 1950. 9 figs., bibliography.

1749. **The Problem of Sporadic Typhus.** (Le problème du typhus sporadique)

R. WORMS. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 4061–4073, Oct. 22, 1950. 3 figs., bibliography.

Three cases of epidemic typhus with a high serological titre against *Rickettsia prowazeki* suspensions were admitted to one hospital in Paris over a period of 18 months. The first patient, a man of 48, came from North Africa and had resided in Paris for 2 years. The onset was abrupt, and the clinical condition and course of the disease typical. The second patient, a woman aged 60, gave a history of infection acquired 17 years previously in Russia. The third patient, a Pole aged 27, had been in both Auschwitz and Dachau camps, where typhus was rife; after release he had an unidentified fever which lasted for 3 weeks.

[The author quotes other cases which have occurred recently in Paris. The discussion (excellently documented) on "Brill's disease" merits reading in the original; the author agrees with Zinsser in considering the disease as a relapse and not a reinfection.]

W. H. Horner Andrews

1750. **Acute Gastro-enteritis due to *T. vincenti* and *B. fusiformis*.** [In English]

L. M. SANGHVI and P. SUBRAHMANYAN. *Indian Medical Gazette* [*Indian med. Gaz.*] **85**, 437–440, Oct., 1950. 4 refs.

Two outbreaks are described of gastro-enteritis in which in the stools and vomit there were masses of *Treponema vincenti* and fusiform bacilli. A total of 80 cases were seen. Apart from diarrhoea and vomiting, dehydration and collapse were common, and in just over a third of the cases there was suppression of urine. In only 5 was the temperature raised. The symptoms were very similar to those of cholera, but the disease did not appear to be transmitted directly from person to person and no cholera vibrios were seen. Sulphonamides were not effective, and apart from fluids given to overcome dehydration the only good results were obtained from injections of oxophenarsine hydrochloride or acetarsol. Arsenicals produced a rapid improvement, the specific organisms disappearing within 24 hours.

G. M. Findlay

1751. **Treatment of Schistosomiasis Mansoni with Antimony Lithium Thiomalate (Anthiomaline): Final Report**

R. RODRIGUEZ-MOLINA, C. E. ACEVEDO, J. M. TORRES, U. LOPEZ-SANABRIA, and E. RAMIREZ-RODRIGUEZ. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **30**, 881–886, Nov., 1950. 7 refs.

The treatment of 39 cases of schistosomiasis mansoni with "anthiomaline" (antimony lithium thiomalate) is described. Anthiomaline contains 10 mg. of tervalent antimony per ml.; it was given by intramuscular injection in doses of 3 ml. on alternate days to a total of 30 ml. The subjects were Puerto Rican recruits to the U.S. Army, in all of whom ova of *Schistosoma mansoni* had been found by the Rivas acid–ether concentration technique. There were no symptoms in 20 of the patients, while the other 19 had low abdominal pain and occasional looseness of stools, rarely with blood. Toxic manifestations in the form of local pain referred from site of injection along a limb, or shoulder pain, occurred in 15 cases. One patient developed desquamation of the skin of hands and feet.

Although in all but one case examination of the faeces was negative, by the end of the course ova were found in two-thirds of the 30 cases followed up for 17 months. It is concluded that anthiomaline in these doses is not very effective in this disease. *Clement Chesterman*

1752. **Psychoneurotic Disturbances in Filariasis, and their Relief by Removal of Adult Worms or Treatment with Hetrazan**

M. KENNEY and R. HEWITT. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **30**, 895–899, Nov., 1950. 12 refs.

The authors consider it is a well-established fact that the central nervous system is subject to allergic disease. They describe 2 cases of loaiasis in whites from the Belgian Congo and 2 cases in negroes from the West Indies, all presumably infected with *Wuchereria bancrofti*, which they regard as examples of psychoneurosis of filarial origin. After the extraction of 4 adult worms in the first case and 6 in the second, the eosinophil count fell from over 50% to less than 5% of the total leucocyte count, and morbid personality changes rapidly vanished. Similar results were obtained by "hetrazan" treatment in the other 2 cases.

[The authors' argument would be more convincing if figures were given comparing the incidence of psychoneurosis in infected and non-infected sections of the population. The fact that one patient had a strong phobia for worms from childhood scarcely favours the allergic hypothesis.] *Clement Chesterton*

History of Medicine

1753. **The Treatment of Head Injuries in France in the Early Seventeen Hundreds, with a Note on Pierre Boudou and his Recognition and Treatment of Subdural Hematoma**
W. PICKLES. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **24**, 421–433, Sept.–Oct., 1950. 1 fig., 9 refs.

After reviewing the early struggles of the surgeons of France to gain public recognition, the author describes the treatment of head injuries in the 18th century, his source of information being the first volume of the Memoirs of the Royal Academy of Surgery (1743).

This little duodecimo volume contains a summary on the use of the trepan in head injuries written by François Quesnay, Secretary of the Academy. Quesnay showed a wide knowledge of the current literature of his time on the symptomatology and management of head injuries. Trepanning was generally recommended for fracture of the skull, but its value was doubtful in cases of headache and of blows upon the head without obvious lesions of the skull. Bleeding was the sovereign remedy for head injuries, with emetics, enemata, and purges as adjuncts. Wounds were treated with dry feathers or pledgets soaked in wine or honey, and the margins held together either by bandages or plasters, or sutures, but sometimes wounds were kept deliberately open. Haematomata and septic swellings of the head were evacuated by incision of the pericranium. Basal fractures were regarded as invariably fatal.

Quesnay reported a case admitted to the Hotel Dieu, Paris, one day after a fall. The patient was under the care of Pierre Boudou (1673–1751), chief surgeon to the hospital. After evacuation of a scalp haematoma improvement occurred, but later trepanning and incision of the dura with escape of blood became necessary. The author regards this as a case where correct diagnosis of subdural bleeding was made and successfully treated, though death followed later from liver abscess. The known publications of Boudou are listed in an appendix.
H. P. Tait

1754. **The Contributions of David Livingstone as a Medical Scientist**
E. H. HUME. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **24**, 434–440, Sept.–Oct., 1950. 2 refs.

When David Livingstone was sent by the London Missionary Society to Africa in 1841 he went out with three aims: to make friends with tribal chiefs, to help in destroying the slave trade, and to fight the widespread and devastating African fevers.

Many of the biological observations made during his explorations were on insects and their relation to disease in animal and man. He remarked that in areas where the scavenger beetle abounded the native villages were sweet and clean. The tsetse fly was accurately described, and Livingstone noted its prevalence along the banks of the Zambesi and that there was a definite "fly belt" in Africa. The bite of the tsetse was observed to be fatal to domestic animals such as oxen, horses, and dogs, but game and goats were unaffected. Livingstone advanced the theory that the tsetse was the cause of nagana (animal trypanosomiasis) and was the first to administer arsenic to horses as a remedy. He recognized that malaria was most prevalent where the mosquito flourished and he evolved a remedy still used in some parts of Africa. This remedy, a mixture of jalap, rhubarb, calomel, quinine, and aloes—"Livingstone's rouser"—was tried out on his infant son, Thomas. Livingstone himself had his first attack of malaria in 1853, and after submitting himself to treatment by native doctors without benefit, he concluded he could cure himself quicker than they could with their native concoctions.
H. P. Tait

1755. **Scientific Work of Paul Gerson Unna. In Commemoration of the One Hundredth Anniversary of his Birth**
A. HOLLANDER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **62**, 351–361, Sept. 1950. 18 refs.

1756. **The Literary and Historical Aspects of the Writings of Sir William Osler**
W. WHITE. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 465–470, Sept. 23, 1950. 18 refs.

1757. **Albert Freeman Africanus King (1841–1914). His Theory as to the Transmission of Malaria by Mosquitoes**
W. B. DANIELS. *Medical Annals of the District of Columbia* [*Med. Ann. Distr. Columbia*] **19**, 499–505 and 542, Sept., 1950. 2 figs., 10 refs.

1758. **Francois Ranchin: Contributor of an Early Chapter in Geriatrics**
J. T. FREEMAN. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **5**, 422–431, Autumn, 1950. 1 fig., 8 refs.

1759. **Giovanni Battista Morgagni (1682–1771) in the History of the Evolution of Medicine**
A. CASTIGLIONI. *Scientia Medica Italica* (*English edition*) [*Sci. med. ital.* (*Engl. ed.*)] **1**, 171–179, 1950.

1760. **Carlo Forlanini and his Contribution to the Therapy of Tuberculosis**
A. CASTIGLIONI. *Scientia Medica Italica* (*English edition*) [*Sci. med. ital.* (*Engl. ed.*)] **1**, 351–363, 1950. 14 refs.

1761. **Sergej Sergeevich Korsakov (1854–1900).** (Сергей Сергеевич Корсаков (1854–1900))
M. O. GUREVICH. Клиническая Медицина [*Klin. Med., Mosk.*] **28**, No. 7, 24–27, 1950. 1 fig.